Irritability Without Elation in a Large Bipolar Youth Sample: Frequency and Clinical Description

JEFFREY HUNT, M.D., BORIS BIRMAHER, M.D., HENRIETTA LEONARD, M.D., MICHAEL STROBER, PH.D., DAVID AXELSON, M.D., NEAL RYAN, M.D., MEI YANG, M.S., MARYKAY GILL, R.N., JENNIFER DYL, PH.D., CHRISTIANNE ESPOSITO-SMYTHERS, PH.D., LANCE SWENSON, PH.D., BENJAMIN GOLDSTEIN, M.D., PH.D., TINA GOLDSTEIN, PH.D., ROBERT STOUT, PH.D., AND MARTIN KELLER, M.D.

ABSTRACT

Objective: To determine whether some children with bipolar disorder (BP) manifest irritability without elation and whether these children differ on sociodemographic, phenotypic, and familial features from those who have elation and no irritability and from those who have both. **Method:** Three hundred sixty-one youths with BP recruited into the three-site Course and Outcome of Bipolar Illness in Youth study were assessed at baseline and for most severe past symptoms using standardized semistructured interviews. Bipolar disorder subtype was identified, and frequency and severity of manic symptoms were quantified. The subjects were required to have episodic mood disturbance to be diagnosed with BP. The sample was then reclassified and compared based on the most severe lifetime manic episode into three subgroups: elated only, irritable only, and both elated and irritable. **Results:** Irritable-only and elated-only subgroups constituted 10% and 15% of the sample, respectively. Except for the irritable-only subjects being significantly younger than the other two subgroups, there were no other between-group sociodemographic differences. There were no significant between-group differences in the BP subtype, rate of psychiatric comorbidities, severity of illness, duration of illness, and family history of mania in first- or second-degree relatives and other psychiatric disorders in first-degree relatives, with the exception of depression and alcohol abuse occurring more frequently in the irritability-only subgroup. The elated-only group had higher scores on most *DSM-IV* mania criterion B items. **Conclusions:** The results of this study support the *DSM-IV* A criteria for mania in youths. Irritable-only mania exists, particularly in younger children, but similar to elated-only mania, it occurs infrequently. The fact that the irritable-only subgroup has similar clinical characteristics and family histories of BP, as compared with subgroups with predominant elation, provides support for continuing to consider episodic irritability in the diagnosis of pediatric BP. *J. Am. Acad. Child Adolesc. Psychiatry,* 2009;48(7):730–739. **Key Words:** phenomenology, bipolar disorder, irritability, elation.

Unique, age-specific aspects of the pediatric bipolar disorder (BP) phenotype continue to be debated. According to the *DSM-IV*[1] criteria, irritability and elation are core features of the pathological alteration in affect and mood in the manic phase of BP, but there is no consensus on the differential significance of these symptoms in children and adolescents.[2–12] In this regard, a recent series of reports,[13,14] documenting a

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Drs. Hunt, Dyl, Esposito-Smythers, Swenson, Stout, and Keller are with the Warren Alpert Medical School, Brown University; Drs. Birmaher, Axelson, Ryan, Goldstein, and Goldstein, and Ms. Yang and Gill are with the University of Pittsburgh Medical Center; and Dr. Strober is with the David Geffen School of Medicine, University of California, Los Angeles. Dr. Leonard, now deceased, was with Brown University.

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Correspondence to Jeffrey Hunt, M.D., 1011 Veterans Memorial Parkway, East Providence, RI 02915; e-mail: Jeffrey_Hunt@Brown.edu.

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dramatic rise in the reported cases of bipolar illness among children and teens, underscores growing concern with diagnostic error in this age group and, accordingly, the need for rigorous, empirical research to illuminate unique psychopathological features of these core elements. Whereas some assert that severe, explosive irritability is more common in children with BP than euphoria or elation,[2–5,12] Geller and colleagues,[9,15] taking note of potential overlap in diagnostic symptoms between early childhood bipolar illness and multiple other forms of severe childhood psychopathology, have argued for the diagnostic centrality of elation and/or grandiosity in the research of pediatric BP to minimize risk of diagnostic imprecision.[10] Notably, in a review and meta-analysis of seven studies, with differing methodologies, of juvenile bipolar subjects completed between 1982 and 2004, Kowatch and colleagues report that rates of irritability and elation vary widely across study samples.[16]

In an attempt to define diagnostic boundaries more sharply, Leibenluft and colleagues[17] have operationalized three clinical phenotypes of BP: narrow, intermediate, and broad. Narrow phenotype BP is defined as a child having at least one episode in which full *DSM-IV* criteria are met, including duration criteria and the presence of elation and/or grandiosity. The intermediate phenotype has two subtypes: mania or hypomania not otherwise specified (NOS) (episodes too short to meet *DSM-IV* duration criteria) and irritable mania or hypomania. Broad phenotype children are characterized by chronic irritability and hyperarousal but specifically exclude patients with elation, grandiosity, and decreased need for sleep. Importantly, this same research group has also subtyped irritability according to course (chronic versus episodic) and found that episodic irritability was associated with BP and anxiety, whereas chronic irritability, or broad phenotype, was more closely associated with oppositional defiant disorder (ODD), conduct disorder, and attention-deficit/hyperactivity disorder (ADHD) and possible increased risk to develop major depressive disorder.[18]

Other recent reports further underscore the potential importance of distinguishing irritability and elation within the pediatric bipolar spectrum. Rich and colleagues compared subjects with disruptive behavior disorders and severe mood dysregulation (SMD) to narrow phenotype bipolar subjects and found differences in psychophysiological measures, thus indicating that the biological substrate of irritability may vary between diagnostic groups.[19] Brotman and colleagues have compared parents of youths with disruptive behavior disorders and SMD with parents of youths with narrow phenotype BP, finding that BP was significantly more likely in parents of narrow phenotype BP.[20] Masi and colleagues reported on 136 BP-I patients (40% female subjects) with mean age of 13.5 years who were clinically subtyped into chronic versus episodic course and "prevalent elated" versus "prevalent irritable" and found that elated mood was more frequent in patients with an episodic course, whereas irritable mood was more frequent in patients with a chronic course.[21]

Reflecting these disparate observations and commentary, the National Institute of Mental Health Research Roundtable on Prepubertal Bipolar Disorder[22] has advocated further clinical observational research to extend our knowledge of the correlates and predictive value of these symptoms. Thus, at this time, the differential significance of irritability versus elated mood with regard to factors such as disease course, psychosocial adjustment, nonaffective diagnostic comorbidity, and treatment response remains conjecture.

The main goals of this study were to determine whether mania/hypomania in youths may be manifested with only irritability without elation and whether children with BP who have irritability and no elation differ on sociodemographic, phenomenological, and familial features from those who have elation and no irritability and from those who have both. The most severe lifetime symptoms (at intake or in the past) were chosen because of the increased likelihood that these symptoms would be better remembered by parents and youths. The main hypotheses tested in this study are that, as indicated in the *DSM-IV*, BP may be manifested with irritability without elation and that groups formed based on the presence or absence of irritability or elation will not differ when compared sociodemographically and phenomenologically and with regard to family history during the most severe lifetime manic episode. An absence of a difference between the groups would add support for the equal importance of these symptoms in the diagnosis of BP and support the inclusion of subjects with irritable mania in future research studies of pediatric BP.

The participants were subjects enrolled in the Pittsburgh, Brown, University of California Los Angeles multisite study, Course and Outcome of Bipolar Illness in Youth (COBY), which is investigating the long-term

psychopathological course, outcome, and effectiveness of naturalistic treatment exposure in pediatric BP. The sample is ideally suited for this investigation because of the large sample, the rigorous application of diagnostic criteria, the availability of family history data, and the enrollment of all the subjects in long-term prospective follow-up assessments. Additionally, the large size of the COBY sample allows for the formation of mood-consistent subgroups categorized by the most severe lifetime manic episode that allows for the investigation of the above hypotheses. Because COBY is following all subjects, future studies will be able to evaluate the above-noted hypotheses prospectively and the stability of the manic symptoms over time.

METHOD

Subjects

This report is limited to a subsample of the study ($N = 361$), all of whom were administered the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) Mania Rating Scale (MRS) about the most serious past episode. The study sample of 446 subjects was enrolled at three academic medical centers: Brown University ($n = 144$), University of California Los Angeles ($n = 90$), and University of Pittsburgh Medical Center ($n = 212$). Detailed descriptions of the baseline phenomenology can be found in previously published reports.[23,24] Briefly, most subjects were referred from outpatient programs (66%); 15% of the subjects were recruited from inpatient units, 14% from advertisements, and 5% from other sources. Study inclusion criteria included current age of 7 years 0 months to 17 years 11 months and meets *DSM-IV* criteria for BP-I or BP-II disorder, or the COBY established criteria for BP NOS. Two hundred twenty-six subjects met criteria for BP-I, whereas 20 subjects met criteria for BP-II and 115 for BP-NOS. Because the *DSM* definition of BP-NOS is not operationalized, to avoid entering into the study youths with "soft" BP symptoms, only children with certain minimum duration plus a minimum number of symptoms with and without previous episodes of depression were considered for the diagnosis of BP-NOS. Bipolar disorder NOS was defined as the presence of elated mood, plus two associated manic symptoms, or irritable mood plus three *DSM-IV*-associated manic symptoms, along with a change in the level of functioning, duration of a minimum of 4 hours within a 24-hour period, and at least 4 cumulative lifetime days meeting the criteria. Children and adolescents meeting this more strictly defined BP-NOS have similar but less severe clinical picture, comorbid disorders, family history, and longitudinal outcome than the BP-I subjects.[25,26] Moreover, approximately 25% of these youths diagnosed with BP-NOS converted into BP-I or BP-II over an average period of 2 years.[23]

Study exclusion criteria were current or lifetime *DSM-IV* diagnosis of schizophrenia, mental retardation, autism or severe autistic spectrum disorders, or mood disorders due to substance abuse, a medical condition, or secondary to the use of medications (e.g., corticosteroids). The subjects determined to have a chronologically primary BP with secondary substance abuse disorder were included into the study.

Informed consent was obtained before initiation of the assessment from the subject's parent/guardian and from subjects aged 14 years or older. The study procedures were explained in age-appropriate language to younger subjects, and verbal assent was obtained before the assessment. The institutional review boards at the three centers reviewed and approved the study protocol before enrollment of any subject.

Subject Assessment

Sociodemographics. Socioeconomic status was measured using the Hollingshead four-factor scale.[25] Pubertal status was reported by the subjects aged 10 years and older using the Pubertal Developmental Scale (PDS).[26] Subjects aged 7 to 9 years completed the PDS with their parent's assistance. The PDS ratings were converted into associated Tanner Stages of sexual development.[27] Subjects whose ratings were equivalent to Tanner Stage I or who were younger than age 8 years were considered prepubertal.

Psychiatric Diagnosis. The subjects were assessed by semistructured interviews of the child/adolescent and a parent/primary caregiver (about the subject) by bachelor's, master's, and doctoral degree–level clinicians. Nonmood psychiatric disorders were assessed using the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL).[28] Because the K-SADS-PL only ascertains the presence or absence of symptoms, mood symptom criteria were assessed using the depression section of the K-SADS-Present Episode, 4th Revision, and the K-SADS MRS to more accurately ascertain the severity of mood symptoms.[29] Manic symptoms and severity thresholds were updated to reflect the current thinking regarding evaluation of mania/hypomania in youths.[30] The K-SADS MRS is a 15-item inventory with excellent interrater reliability (intraclass correlation coefficient = 0.97), convergent validity with Clinical Global Impressions Severity Scale ($r_s = 0.91$), and differentiates bipolar patients from those without significant manic symptoms.[31] Items on the K-SADS MRS are derived from the K-SADS-Present Episode 1986 version and include a mood lability item. Symptoms are rated from 1 (normal or not present) to 6 (extreme symptoms). Mild elation (rated as 3 on this scale) reflects the presence of a "definitely elevated mood and optimistic outlook that is somewhat out of proportion to his/her circumstances." Mild irritability (rated as 3 on this scale) reflects the presence of "often (at least 3 times every 3 hours each week) feels definitely more angry, irritable than called for by the situation, relatively frequent but never very intense. Or often argumentative, quick to express annoyance. No homicidal thoughts." (For further information regarding the items included in the K-SADS MRS, see *www.wpic.pitt.edu/research* under "Assessment Instruments.")

Depressive and manic symptom severity ratings were recorded for the most severe week in the month before the intake assessment. The subjects were not required to be in an episode of mania or depression at the time of intake. The most severe week of depressive and manic symptoms in the subject's lifetime was assessed using the K-SADS-PL with the first 84 subjects enrolled in the study and the K-SADS MRS and K-SADS-PL mood disorder sections for the remaining subjects. The subjects were asked about all lifetime mania or hypomanic episodes, but only the most severe and the current (within the last month) were rated. Mood symptoms that overlap with other psychiatric disorders (i.e., motor hyperactivity, distractibility) were not rated as present in the mood sections unless they intensified with the onset of abnormal mood. Comorbid diagnoses were not assigned in COBY if they occurred exclusively during a

mood episode. The onset of the first and the most recent episode of each type of *DSM-IV* major mood episode (manic, mixed, hypomanic, or major depressive episodes) were recorded, as well as the first time the subjects met the criteria for BP-NOS. The age of onset for a subject's BP spectrum illness was defined as the age of onset of clinically significant manic, hypomanic, and/or depressive symptoms that affected the child's functioning. Illness duration was defined as the subject's current age minus the age of BP onset. However, given the controversies diagnosing BP in very young children, the minimum age of onset for BP spectrum illness was arbitrarily set at age 4 years.

All interviewers and doctoral-level clinicians underwent training and certification in the K-SADS at each site. All cases were discussed during weekly clinical consensus team meetings at each site to confirm the diagnoses. This clinical consensus team consisted of doctoral degree–level child and adolescent psychiatrists and/or psychologists and the interviewers. During this meeting, the K-SADS symptoms and the subject's medical records were reviewed. A best estimate clinical consensus procedure was used to confirm the child psychiatric diagnosis.[23,24] Additionally, diagnostic issues that could not easily come to consensus were conferenced across the three sites. There was high reliability for differentiating BP from non-BP subjects ($\kappa = 0.90$) and the BP diagnostic subtypes ($\kappa = 0.79$). For the nonmood disorders, κ's were 0.80 or higher. The intraclass correlation coefficient was 0.96 for the K-SADS MRS and 0.98 for the K-SADS Depression scale.

Global Impairment. The Children's Global Assessment Scale was used to establish global level of functioning.[32] The Children's Global Assessment Scale is a clinician-rated global measure of impairment with excellent interrater reliability.[33] Scores range from 1 to 100 (scores higher than 70 indicate normal adjustment).

Familial Psychiatric Diagnosis. The primary caretaker of the subject was interviewed at intake about his/her personal psychiatric history using the Structured Clinical Interview for *DSM-IV*.[34] In addition, the primary caretaker was interviewed about the psychiatric status of the subject's first- and second-degree relatives using the Family History Screen (FHS).[35] For each disorder, the interviewer indicates which family members were reported as having experienced the disorder, separately for first- and second-degree relatives using a four-point scale (1 = not present, 2 = possible, 3 = probable, and 4 = definite). The disorders examined in the current study were major depression, mania, anxiety disorders, ADHD, ODD, conduct disorder, schizophrenia, eating disorders, substance abuse, substance dependence, and suicidal attempts/completions. The FHS yields acceptable test-retest reliability and validity as determined by comparing informant family history diagnosis to best estimate diagnoses based on direct interview.[35]

DSM-IV "Criterion A" Symptom Subgrouping

To further understand the clinical implications of the symptoms of irritability and elation in the diagnosis of BP, the subjects were classified by primary *DSM-IV* criterion A manic symptoms. Independent of BP subtype, the subjects were classified into one of three symptom subgroups using most serious lifetime manic episode scores on the MRS: elation only, irritability only, and elation plus irritability. The subjects were classified as having elation or irritability if K-SADS MRS scores were rated in the "mild but definite" range (a score of 3) or above. All of the subjects met the consensus criteria for BP based on *DSM-IV* criteria. The subjects with mild category A symptoms still had other impairing symptoms above the clinical threshold and had clear episodicity.

Three hundred sixty-one of the total 446 subjects were classified into one of these three categories. Eighty-five subjects who were enrolled early in the study did not have most serious past episode of mania recorded using the K-SADS MRS, so these subjects were not included in this analysis. The absence of data for these subjects was due to an early change in the COBY methodology (previously described).

Statistical Analyses

SPSS (SPSS Inc., Chicago, IL) was used for data analysis. Differences in demographic, phenomenological, and family history factors among the three symptom groups were analyzed using analysis of variance, χ^2, and nonparametric univariate tests (Kruskal-Wallis test), as required by the characteristics of the data. For comparing K-SADS most serious lifetime manic symptoms, we conducted a multivariate analysis of covariance (MANCOVA) analysis in which age was covaried because the groups were found to differ on this characteristic. In this MANCOVA, the elation and irritability scores that were used to define the groups were omitted. This analysis was used to determine that the groups differed with regard to lifetime symptoms overall. Because the MANCOVA analysis requires listwise case deletion, however, we also analyzed group differences on the K-SADS lifetime symptoms by univariate analysis of covariance, covarying for age. Because both methods yielded similar results, we report the univariate results because the *N*s are higher for these analyses. All values are reported as means ± SDs unless otherwise specified. All p values are based on two-tailed tests with $\alpha = .05$.

RESULTS

Analyses of Criterion A Symptoms

To describe the symptom stability of the three subgroups, we compared the elation and irritability MRS scores at the time of intake and at most serious past manic episode. As previously noted, the subjects did not need to meet criteria for a manic episode at intake to be enrolled in the study. However, all of the subjects met threshold criteria for elation and/or irritability at intake or at most serious past episode. Sixty percent of the subjects met threshold criteria for elation and/or irritability at both intake and at the most serious past episode. Additionally, for the elation-only group, 100% were below threshold criteria for irritability at both time points, and similarly, for the irritable-only group, 100% were below threshold criteria for elation at both time points. Fifty-seven per cent of the elation-only group ($n = 54$) met threshold criteria for high elation at intake and at most serious past episode. Sixty-one percent of the irritability-only group ($n = 36$) met threshold criteria for high irritability at intake and at most serious past episode.

Demographics, Bipolar Subtype, Duration of Symptoms, and Age of Onset. As shown in Table 1, there were no significant differences between these three subgroups in

TABLE 1

Total Sample Comparison by *DSM-IV* Category A Most Severe Lifetime Mania Symptoms: Elation, Irritability, and Elation/Irritability

	All Subjects (N = 361)	Elation Only (n = 54)	Irritability Only (n = 36)	Both Elation and Irritability (n = 271)	Statistics	Overall p
Demographics (% yes or mean ± SD)						
Age, y	12.5 ± 3.3	12.7 ± 3.4[a]	10.5 ± 2.8[b]	12.7 ± 3.3[a]	$F_{2,358}$ = 6.8	.01
Sex, % male	50.7	42.6	44.4	53.1	χ^2_3 = 2.6	.3
Race, % white	79.5	72.2	88.9	79.7	χ^2_3 = 3.7	.2
Ethnic, % Hispanic	6.6	7.4	2.8	7.0	FET	.8
SES	3.4 ± 1.2	3.6 ± 1.2	3.1 ± 1.2	3.3 ± 1.2	$F_{2,358}$ = 1.9	.2
Living with both natural parents, % yes	40.7	37.0	41.7	41.3	χ^2_3 = 0.4	.8
Pubertal status category						
I	28.0	19.0	37.9	28.5	χ^2_6 = 10.6	.03
II–III	25.8	23.8	41.4	24.0		
IV–V	46.1	57.1[a]	20.7[b]	47.5[a]		
Bipolar category						
BP-I	62.6	57.4	44.4	66.1	FET	.1
BP-II	5.5	5.6	8.3	5.2		
BP-NOS	31.9	37.0	47.2	28.8		
Age of onset/duration of illness						
Age of onset of mood symptoms	8.2 ± 4.2	8.3 ± 4.4	6.8 ± 3.4	8.4 ± 4.2	KW χ^2_3 = 3.6	.2
Age of onset of BP-spectrum illness (minimum 4)	9.2 ± 4.0	9.6 ± 4.3	8.2 ± 3.3	9.2 ± 4.0	KW χ^2_3 = 2.3	.3
Duration of BP-spectrum illness	3.3 ± 2.6	3.1 ± 2.6	2.4 ± 1.7	3.4 ± 2.7	$F_{2,358}$ = 2.9	.05
Symptom severity—most severe week during month before intake						
MRS score—current	22.9 ± 12.3	21.5 ± 13.4	20.7 ± 9.5	23.5 ± 12.4	KW χ^2_3 = 2.9	.2
MRS score—most serious lifetime	33.8 ± 8.3	30.9 ± 8.2[a]	28.5 ± 7.6[a]	35.1 ± 8.0[b]	$F_{2,356}$ = 15.3	<.001
DEP-P score—current	14.6 ± 10.1	15.5 ± 10.0	14.4 ± 10.8	14.5 ± 10.1	$F_{2,354}$ = 0.2	.8
DEP-P—most serious lifetime	22.7 ± 11.0	23.1 ± 11.5	19.0 ± 9.7	23.1 ± 11.0	$F_{2,352}$ = 2.3	.10
Functional impairment						
CGAS-current	53.6 ± 11.6	53.7 ± 12.5	53.4 ± 11.4	53.7 ± 11.5	$F_{2,354}$ = 0.01	1.0
CGAS most serious lifetime	37.7 ± 9.9	37.9 ± 10.8	39.9 ± 6.7	37.4 ± 10.1[b]	KW χ^2_3 = 1.7	.4
Lifetime history of comorbid disorders (% yes)						
Lifetime any anxiety disorder	39.1	35.2	36.1	40.2	χ^2_3 = 0.6	.7
Lifetime panic disorder	4.4	1.9	5.6	4.8	FET	.6
Lifetime SAD	24.1	20.4	22.2	25.1	χ^2_3 = 0.6	.7
Lifetime social phobia	5.3	11.1	2.8	4.4	FET	.1
Lifetime GAD	12.7	14.8	2.8	13.7	FET	.1
Lifetime OCD	6.1	5.6	2.8	6.6	FET	.8
Lifetime PTSD	6.6	1.9	11.1	7.0	FET	.2
ADHD	60.7	59.3	69.4	59.8	χ^2_3 = 1.3	.5
Conduct disorder	12.5	7.4	22.2	12.2	FET	.1
ODD	38.0	35.2	25.0	40.2	χ^2_3 = 3.3	.2
Substance/alcohol, abuse or dependence	8.9	9.3	2.8	9.6	FET	.4
Lifetime phenomenological features, % yes						
Psychosis	20.2	22.2	11.1	21.0	χ^2_3 = 2.1	.4
Lifetime major depressive episode	47.1	55.6	36.1	46.9	χ^2_3 = 3.3	.2
Suicidal ideation	75.1	75.9	77.8	74.5	χ^2_3 = 0.2	.9
Suicidal attempt	28.3	25.9	13.9	30.6	χ^2_3 = 4.6	.1
Self-injurious behavior	41.7	44.4	38.9	41.5	χ^2_3 = 0.3	.9
Psychiatric hospitalization	47.8	48.1	38.9	48.9	χ^2_3 = 1.3	.5
Psychotropic medication	94.5	92.6	94.4	94.8	FET	.7
Medication	97.2	98.1	94.4	97.4	FET	.5

TABLE 2
Comparison of Family History by *DSM-IV* Category A Most Severe Lifetime Mania Symptoms: Elation, Irritability, and Elation/Irritability

	All Subjects (N = 361)	Elation Only (n = 54)	Irritability Only (n = 36)	Both Elation and Irritability (n = 271)	Statistics	Overall p
Any first family history with lifetime disorder (% yes)						
Depression	75.7	80.4	69.7	75.5	$\chi^2_3 = 1.3$	.5
Mania/Hypomania	38.6	29.4	34.4	41.0	$\chi^2_3 = 2.7$	.3
ADHD	35.6	38.0	40.6	34.4	$\chi^2_3 = 0.9$	.6
Conduct disorder	23.3	24.0	21.9	23.3	$\chi^2_3 = 0.04$	1.0
Schizophrenia	1.2	2.0	0.0	1.2	$\chi^2_3 = 1.0$	.6
Anxiety	55.6	54.9	50.0	56.5	$\chi^2_3 = 0.4$	.8
Substance/alcohol abuse	31.9	31.4	21.2	33.5	$\chi^2_3 = 2.1$	.4
Substance/alcohol dependence	33.4	25.5	47.1	33.2	$\chi^2_3 = 4.3$	.1
Suicidal attempt or completion	23.7	25.5	21.2	23.7	$\chi^2_3 = 0.2$	.9
Any second family history with lifetime disorder (% yes)						
Depression	69.9	62.0[a]	87.1[b]	69.4[a]	$\chi^2_3 = 6.5$	.04
Mania/hypomania	38.6	26.0[a]	48.4[b]	39.9[b]	$\chi^2_3 = 5.4$	.07
ADHD	31.5	26.5	32.3	32.4	$\chi^2_3 = 0.8$	.7
Conduct disorder	26.5	28.6	25.8	26.1	$\chi^2_3 = 0.1$	1.0
Schizophrenia	5.6	6.0	3.2	5.8	$\chi^2_3 = 0.6$	.7
Anxiety	49.1	56.0	58.1	46.5	$\chi^2_3 = 2.4$	.3
Substance/alcohol abuse	47.7	46.0	45.2	48.4	$\chi^2_3 = 0.4$	.8
Substance/alcohol dependence	46.6	34.0[a]	67.7[b]	46.6[a]	$\chi^2_3 = 9.0$	.01
Suicidal attempt or completion	32.0	30.0	38.7	31.6	$\chi^2_3 = 0.7$	.8

Note: Values with different superscripts are significant at $p \leq .05$; controlling for the number of relatives. ADHD = attention-deficit/hyperactivity disorder.

terms of sex, race, living arrangements, socioeconomic status, or ethnicity. However, the subjects with irritability only were significantly younger and had earlier pubertal status than the subjects with elation only and the subjects with both elation and irritability. There were no significant between-group differences in BP subtype, age of onset of mood symptoms, age of onset of BP, or duration of BP. There was a trend for the irritability-only subjects to be more represented among those with BP-NOS. The subjects with elation plus irritability and elation only had significantly higher K-SADS MRS most serious lifetime mania compared with the irritability-only subgroups. In a secondary analysis, the specific MRS elation and irritability symptom scores were omitted from this recalculation, and the results similarly indicated that the irritable-only subjects had significantly lower total MRS scores than the other two groups, $F_{2,357} = 5.5$, $p = .005$.

Comorbidity and Lifetime Phenomenological Features. There were no significant differences between the symptom subgroups when comparing percent positive lifetime history of ADHD, ODD, conduct disorder, substance abuse, and anxiety disorders. There was also no effect of *DSM-IV* criterion A symptom profile on

Table 1 Note: Age of onset of BP spectrum illness is set age 4 years as the minimum. Lifetime anxiety includes panic disorder, SAD, social phobia, GAD, OCD, and PTSD. Values with different superscripts are significant at $p \leq .05$. ADHD = attention-deficit/hyperactivity disorder; BP-I = bipolar 1 disorder (as defined by the *DSM-IV-TR*); BP-II = bipolar 2 disorder (as defined by the *DSM-IV-TR*); BP-NOS = bipolar NOS disorder (as defined by the COBY study noted in the body of the text); C-GAS = Children's Global Assessment Scale; DEP-P = depression section of the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version; FET = Fisher exact test; GAD = generalized anxiety disorder; KW = Kruskal-Wallis test; MRS = Mania Rating Scale of the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version; OCD = obsessive-compulsive disorder; ODD = oppositional defiant disorder; PTSD = posttraumatic stress disorder; SAD = separation anxiety disorder; SES = socioeconomic status.

TABLE 3

Comparison of K-SADS Most Serious Lifetime Manic Symptoms by *DSM-IV* Category A Mania Symptoms: Elation, Irritability, and Elation/Irritability

	All Subjects (N = 361)	Elation Only (n = 54)	Irritability Only (n = 36)	Both Elation and Irritability (n = 271)	Statistics	Overall p
Grandiosity	3.3 ± 1.4	3.5 ± 1.5[a]	2.6 ± 1.4[b]	3.3 ± 1.4[a]	$F_{2,359}$ = 3.5	.03
Decreased need for sleep	4.0 ± 1.9	4.6 ± 1.6[a]	2.8 ± 1.9[b]	4.0 ± 1.8[a]	$F_{2,358}$ = 9.0	<.0001
Accelerated speech	4.1 ± 1.2	4.0 ± 1.4	3.6 ± 1.3	4.2 ± 1.1	$F_{2,359}$ = 2.2	.11
Racing thoughts	3.4 ± 1.6	3.5 ± 1.6	2.7 ± 1.6	3.7 ± 1.6	$F_{2,358}$ = 2.0	.14
Flight of ideas	3.5 ± 1.4	3.1 ± 1.5[a]	2.8 ± 1.5[a]	3.7 ± 1.3[b]	$F_{2,354}$ = 9.7	<.0001
Distractibility	3.5 ± 1.1	3.4 ± 1.2	3.4 ± 1.2	3.5 ± 1.1	$F_{2,358}$ = 0.5	.6
Increased goal-directed activity	3.0 ± 1.6	3.4 ± 1.7[a]	2.1 ± 1.3[b]	3.1 ± 1.5[a]	$F_{2,358}$ = 4.86	.01
Motor hyperactivity	4.3 ± 1.1	4.2 ± 1.3	4.1 ± 1.2	4.4 ± 1.1	$F_{2,355}$ = 1.4	.3
Poor judgment	3.9 ± 1.6	3.4 ± 1.7[a]	3.9 ± 1.5[b]	3.9 ± 1.5[b]	$F_{2,359}$ = 3.0	.05
Unusual energy	4.5 ± 1.3	4.7 ± 1.3[a]	3.8 ± 1.7[b]	4.6 ± 1.2[a]	$F_{2,358}$ = 3.8	.02
Hallucinations	1.8 ± 1.3	1.8 ± 1.4	1.5 ± 0.9	1.9 ± 1.4	$F_{2,356}$ = 1.5	.2
Delusions	1.4 ± 0.9	1.5 ± 1.1	1.1 ± 0.4	1.4 ± 1.0	$F_{2,352}$ = .98	.4
Mood lability	4.1 ± 1.1	3.4 ± 1.3[a]	4.6 ± 1.0[b]	4.2 ± 1.0[c]	$F_{2,353}$ = 13.39	<.0001
Inappropriate laughing	2.8 ± 1.1	2.9 ± 1.0[a]	2.3 ± 1.2[b]	2.9 ± 1.0[a]	$F_{2,357}$ = 4.9	.001
Uninhibited people seeking	2.5 ± 1.2	2.4 ± 1.1	2.2 ± 1.1	2.5 ± 1.2	$F_{2,357}$ = 0.66	.5
Increased productivity	2.2 ± 1.2	2.5 ± 1.2	1.9 ± 1.0	2.3 ± 1.2	$F_{2,358}$ = 1.8	.2
Sharpened creative thinking	2.3 ± 1.1	2.3 ± 1.1	1.8 ± 1.0	2.3 ± 1.1	$F_{2,353}$ = 2.2	.1
Hypersexuality	2.3 ± 1.2	2.1 ± 1.1	2.3 ± 1.2	2.3 ± 1.3	$F_{2,356}$ = 0.6	.5
Sentence incoherence	1.7 ± 1.1	1.4 ± 1.0	1.7 ± 1.1	1.7 ± 1.2	$F_{2,357}$ = 1.2	.3
Derailment	1.5 ± 1.0	1.5 ± 1.0	1.6 ± 1.1	1.6 ± 1.1	$F_{2,356}$ = 0.3	.7

Note: Values with different superscripts are significant at $p \leq .05$; multivariate analysis-MANCOVA (controlling for age). K-SADS = Schedule for Affective Disorders and Schizophrenia for School-Age Children.

the lifetime presence of psychosis, suicidal ideation, suicide attempt, self-injurious behavior, psychiatric hospitalizations, or exposure to psychopharmacological medication.

Family History. As shown in Table 2, after adjusting for the number of members within each family, there were no effects of *DSM-IV* criterion A symptom profile on rates of familial psychiatric illness in first-degree relatives. This was also the case for second-degree relatives, with the exception of depression and alcohol dependence. The irritability-only subgroup had significantly more second-degree family history of depression and alcohol dependence compared with the elation-only subgroup. There was also a trend toward more second-degree relatives with mania in the irritability-only group.

MRS Scores. As depicted in Table 3, there were many significant differences, after controlling for age and analysis using MANCOVA, in mean K-SADS MRS for individual symptoms among the three symptom subgroups. The elation-only and elation+irritability subgroups had higher scores on the K-SADS MRS items than the irritability-only subgroup for the following symptoms: grandiosity, decreased need for sleep, increased goal-directed activity, inappropriate laughing, and unusual energy. The elation+irritability subgroup had significantly higher K-SADS MRS scores than the irritability-only group for increased creativity. The irritability-only subgroup had significantly higher mood lability K-SADS MRS scores than the elation-only and the elation+ irritability subgroups.

The frequency of grandiosity within each subgroup using the same cutoff scores (3 and above = present and 2 and below = not present) was analyzed. We found that 71% of the entire sample had mild or greater most serious lifetime grandiosity scores on the MRS, whereas 74% of the elation-only, 56% of the irritability-only, and 73% of the elation+irritability subjects had mild or above most serious lifetime grandiosity scores on the MRS. The three groups did not differ significantly on grandiosity score (χ^2_2 = 5.324, p = .07).

We have also analyzed the sample using just the current (K-SADS MRS at intake) episode. There were no significant differences between the reclassified symptom

subgroups when compared by bipolar subtype, severity of disorder at baseline, percent comorbid conditions, or family history in this analysis.

DISCUSSION

The main goals of this study were to determine whether mania/hypomania in youths may be manifested with only irritability without elation and whether children with BP who have irritability and no elation differ on sociodemographic, phenomenological, and familial features from those who have elation and no irritability and from those who have both. We found that irritable-only mania and elated-only mania constituted 10% and 15% of the sample, respectively, with the majority having both elation and irritability. However, it is important to highlight that only the most severe lifetime manic episode symptoms that occurred at intake or in the past were analyzed. Thus, it is possible that the current grouping of "irritability-only" bipolar children might have experienced an elated mania during another, although less severe, episode (and vice versa for the "elation-only" bipolar children). Except for the irritable-only subjects being significantly younger than the other two subgroups, there were no other between-group sociodemographic differences. There were also no significant between-group differences in the bipolar subtype, rate of psychiatric comorbidities, severity of illness, and duration of illness. Importantly, we found that the three subgroups, (irritability only, elation only, and elation plus irritability), did not differ with regard to family history of psychiatric disorders in first-degree relatives. Rates of disorder in second-degree relatives were also similar between the three subgroups with the exception of depression and alcohol abuse occurring more frequently in the irritability-only subgroup. Taken together, these findings indicate that the *DSM-IV* A criteria is applicable to youths with BP and that the irritability-only subgroup, who in COBY also have distinct mood episodicity, is generally not significantly different from groups with elation, supporting continuing to consider irritability as a mood symptom in the diagnosis of juvenile BP. These results also do not support previous research, which suggests that irritability alone is the most common presentation of mania in children and adolescents.[12]

The presence of elation was associated with higher scores on most *DSM-IV* mania criterion B items. The elation-only and elation+irritability subgroups had higher individual scores on the K-SADS MRS items than the irritability-only subgroup. In this way, the elation subgroups seem similar to the "narrow" phenotype defined by Leibenluft and colleagues[17] and also similar to the subjects included in the sample by Geller and colleagues[9,10] as well as that of Masi and colleagues.[21] The irritability-only subgroup seems to be most similar to the "intermediate phenotype" subjects also described by Leibenluft and colleagues.[18,19] More than half (56%) of these irritable-only subjects would have been included in the studies by Geller et al.[9,10] because of the presence of grandiosity. The irritability-only subgroup defined in this study would not be considered similar to children referred to by Leibenluft and colleagues[18,20,36] as "SMD" because SMD subjects by definition do not have mood episodes but chronic symptoms, most fulfill the *DSM-IV* criteria for ODD/conduct disorder/ADHD, and do not fulfill the criteria for any *DSM-IV* BP subtype, including COBY's modification of the *DSM-IV* BP-NOS.[23,24]

The finding that the subjects with BP who were in the irritable-only subgroup did not differ from the two groups with elation in terms of frequency of family history of psychopathology is important. Brotman and colleagues reported that narrow phenotype BP may be distinct from SMD in terms of familial aggregation of psychiatric illness.[21] The fact that the irritable-only subjects in COBY did not differ from the subjects with elation may be explained by the necessity for mood episodicity in COBY's inclusion criteria. This emphasizes the importance of considering episodicity when diagnosing youths with BP, particularly if they do not have elation.

We found that approximately 75% of the sample had both elation and irritability, whereas 15% had elation with no irritability, and 10% were defined as having irritability without elation. These results suggest that irritability and elation most often co-occur, which is consistent with other groups.[10,11,21] It is also striking to note that the irritability-alone group was significantly younger and that they had lower MRS scores on most items. These differing clinical presentations between children and adolescents may be attributable, at least in part, to the psychosocial and maturational changes that occur after puberty.[30] Although speculative, it is possible

that the younger age associated with the irritable-only subgroup may be at least partially accounted for by their earlier developmental stage encompassing more predominant subcortical limbic mechanisms and less advanced prefrontal cortex operations in which mania is manifested by more diffuse irritability instead of elated mood, which may require the acquisition of more complex neurodevelopmental processes.[37,38] It will be of interest to see if these differences are just due to age and to see if this group will eventually begin to appear phenomenologically more similar to the other two groups or if they will remain different.

The results of the study must be considered in the context of certain limitations. The symptoms obtained from the most severe lifetime manic episode were subject to retrospective bias. Only the most severe lifetime manic episode symptoms were analyzed, thus missing possibly important retrospective clinical data from other episodes. Because COBY is following all of the subjects, longitudinal follow-up of this sample will more accurately account for all subsequent episodes of mood disturbance and evaluate the stability of the manic symptoms over time and whether more subjects present with only irritable mania. An additional limitation is that the family history method (FHS) used may underestimate the occurrence of disorders in relatives (especially second-degree relatives) compared with direct interviews of family members. However, previous COBY studies have found that the FHS was able to discriminate clinical subgroups.[39,40] Finally, the study sample was recruited by a variety of methods including referral from clinical programs. Therefore, the subjects may represent a more severely affected cohort of bipolar youths, and thus, results may not generalize to an epidemiological sample of bipolar youths. It could also be that the chance of referral would differ depending on irritability versus elation status. Finally, another limitation is that most of the subjects were white, which may limit generalizability.

The results of this study support the *DSM-IV* A criteria for mania in youths. Our results also support previous findings that most youths with BP have elation co-occurring with irritability with a small percentage, particularly among younger children, having irritability only. The fact that the irritable-only subgroup in this study has similar clinical characteristics and family histories of BP, as compared with the subgroups with predominant elation, provides support for continuing to consider irritability in the diagnosis of juvenile BP, particularly if they have episodic illnesses and other *DSM-IV* category B symptoms. Longitudinal follow-up of this sample will clarify whether the presence of predominance of elation or of irritability at baseline will be predictors of future clinical outcomes.

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