Outpatient Diagnosis and Clinical Presentation of Bipolar Youth

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ABSTRACT

Introduction: Many children and adolescents in the community do not fit the classic Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) criteria for Bipolar Disorder, Type I., and bipolar disorder, not otherwise specified (BPNOS) is often the "catch all" diagnosis. Significant research has been conducted to better understand the phenomenology of the spectrum of bipolar disorder; however, there are presently different operational definitions for bipolar disorder, in both clinical and research settings. A recent study, The Course and Outcome of Bipolar Youth (COBY) provided preliminary validation for diagnosing BPNOS. Using these COBY research definitions for BPNOS, we examined the clinical presentation and the prior history of psychotropic medication usage of youth with BPI vs. BPNOS presenting to an outpatient clinic. **Methods:** The initial evaluation consisted of a direct clinical interview with the parent(s) and the patient. Standardized rating scales such as the Young Mania Rating Scale and the Quick Inventory of Depressive Symptoms were used to assess current mood states. The Clinical Global Impressions Scale-Severity was used to assess the overall functioning of bipolar youth. **Results:** Age, comorbidities, and family histories of 68 bipolar youth in the clinic are similar to what other studies have reported. BPNOS youth have significant functional impairment which is comparable to the BPI youth. Both bipolar groups are equally likely to have similar prior exposure to psychotropic medications. **Discussion:** BPNOS is a serious illness the diagnostic guidelines for which are still debatable. Until further clarification of this diagnosis, the COBY definitions for BPNOS can be used in a clinic. The use of stringent criteria for diagnosing the bipolar spectrum disorders allows for careful differential diagnoses of psychiatric illnesses.
Key words: bipolar, outpatient, diagnosis

RÉSUMÉ

Introduction: Les nombreux enfants et adolescents qui ne présentent pas les symptômes classiques du trouble bipolaire de type 1 reçoivent souvent un diagnostic *fourre-tout* de trouble bipolaire non spécifié. En dépit des différentes définitions du trouble bipolaire utilisées actuellement en clinique ou en recherche, la phénoménologie des diverses manifestations de ce trouble fait l'objet de travaux de recherche significatifs. La récente étude intitulée *The Course and Outcome of Bipolar Youth (COBY)* propose une validation préliminaire du diagnostic de trouble bipolaire non spécifié. Nous basant sur les définitions données dans cette étude, nous avons comparé, chez des enfants et adolescents qui se sont présentés en clinique externe, les symptômes cliniques du trouble bipolaire de type 1 à ceux du trouble bipolaire non spécifié. Les psychotropes prescrits dans les deux cas ont également été comparés. **Méthodologie:** L'évaluation initiale a consisté en une entrevue clinique directe avec le patient et le ou les parents. L'humeur des patients a été évaluée au moyen de la *Young Mania Rating Scale* et du *Quick Inventory of Depressive Symptoms,* le fonctionnement global au moyen du *Clinical Global Impressions Scale-Severity*. **Résultats:** Les données comme l'âge, les comorbidités et les antécédents familiaux de 68 enfants et adolescents bipolaires sont identiques à celles indiquées dans d'autres études. Les sujets des deux groupes (trouble bipolaire de type 1 et trouble bipolaire non spécifié) affichent des troubles du fonctionnement comparables. L'exposition passée aux psychotropes est censée être identique pour les deux groupes. **Discussion:** Les directives se rapportant au diagnostic du trouble bipolaire non spécifié, qui est une maladie grave, sont discutables. Dans l'attente d'une clarification de ce diagnostic, il est possible d'utiliser, dans la pratique clinique, les définitions données dans l'étude *COBY.* L'application de critères plus rigoureux au diagnostic des divers types de trouble bipolaire permettra d'améliorer le diagnostic différentiel de ce trouble.
Mots-clés: trouble bipolaire, clinique, diagnostic

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Introduction

Many children and adolescents in the community do not fit the classic Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR; APA 2000) criteria for Bipolar Disorder, Type I (BPI; Lewinsohn et al., 1995). Indeed, studies indicate that most youth presenting to community practitioners have either an inadequate duration of symptoms of pediatric bipolar disorder (PBD), an insufficient number of symptoms or are chronically irritable (Leibenluft, Charney, Towbin, Bhangoo, & Pine, 2003). In clinical practice, these youth may be diagnosed as having bipolar disorder, not otherwise specified (BPNOS).

Although significant research has been conducted to better understand the phenomenology of bipolar disorder, there are presently different operational clinical and research definitions for BPNOS (Youngstrom et al., 2008). The National Institute of Mental Health (NIMH) funded a study, The Course and Outcome of Bipolar Youth (COBY) study, which not only assessed the clinical presentation, family history and longitudinal course of children

and adolescents with bipolar spectrum disorders (BP type I, BP type II and BPNOS), but also provided anchors for the diagnosis of BPNOS (Axelson et al., 2006; Birmaher et al., 2006).

We have developed a PBD specialty outpatient clinic which provides diagnostic evaluations and treatment for bipolar children and adolescents. Because the results of the COBY study provided preliminary validation for BPNOS (Birmaher et al., 2006) these research definitions for diagnosing BPNOS were utilized in the PBD clinic. The children and adolescents in the PBD clinic were assessed via a direct clinic interview to establish the diagnosis. Standardized mood rating scales were used to assess symptom severity at the initial interview.

Specifically, the aims of this paper are as follows:

- Aim 1: Using the COBY research definitions for BPNOS, we examine the clinical presentation of youth with BPI vs. BPNOS presenting to an outpatient bipolar clinic.
- Aim 2: To assess the prior history of psychotropic medication usage for both the BPNOS and the BPI youth.

Methods

Pediatric Bipolar Disorders Outpatient Clinic

The Pediatric Bipolar Disorders Outpatient specialty clinic was developed as part of the Child and Adolescent Psychiatry Outpatient Clinic at Children's Medical Center (CMC) in Dallas. This clinic utilizes standardized measures of mood and overall functioning to assess mood symptoms at each visit. This clinical information and medication changes are documented in a clinical database.

Bipolar Diagnosis

Patient referrals come from pediatricians, psychiatrists, other mental healthcare providers, schools in the community, and self-referrals. All youth referred to the PBD clinic are evaluated by a child psychiatry fellow and the attending psychiatrist (KS). This evaluation consists of a direct clinical interview with the patient and his/her parent(s) or primary caregiver. Additional information from the child's school teachers is obtained, if required. We used the DSM-IV-TR criteria for making the diagnosis of BPI and BPII, and the COBY research criteria for diagnosing BPNOS.

Patients

In the PBD clinic we either confirm or make a diagnosis of bipolar disorder in the child/adolescent presenting to the clinic. Those diagnosed with bipolar disorder continue to receive treatment in the PBD clinic if the family so wishes. Those receiving other psychiatric diagnoses are either seen in our general outpatient clinic or referred to other providers in the community. Since the inception of the PBD outpatient clinic, 221 youth have been assessed for bipolar disorder. Of these, 85 children and adolescents (aged 3-17 years) were diagnosed with bipolar disorder: 53 with BPNOS, 30 with BPI, and 2 with BPII.

The current study evaluated the baseline characteristics of BPI and BPNOS youth aged 7-18 years. Thus, 68 bipolar youth were included in the current study: 29 BPI youth and 39 BPNOS youth.

The Institutional Review Board at UT Southwestern Medical Center approved the collection and publication of this clinic data. This was a retrospective study.

Demographic and Baseline Clinical Measures

Demographics, i.e. age, gender, and ethnicity of bipolar youth were obtained at baseline.

The severity of mood symptoms of the bipolar youth were assessed using the Young Mania Rating Scale (YMRS; Young et al., 2006), and the Quick Inventory of Depressive Symptomatology (QIDS; Rush et al., 2003). The Young Mania Rating Scale (YMRS) is an eleven-item, clinician administered rating scale used to measure the severity of manic symptoms in children and adolescents between the ages of 5 and 17, during the past 7 days. The range of scores is from 0-56. A score of 12 and above is considered hypomania and mania. The Quick Inventory of Depressive Symptomatology, Adolescent Version (QIDS-A_{17}) was adapted from the $QIDS_{16}$ for use with adolescents (Haley et al., 2009). The $QIDS_{16}$ has anchor points that specify the severity and frequency of symptoms and provide equivalent

Table 1: The COBY criteria for BPNOS (Axelson et al., 2006**) are defined as follows:**

Children and adolescents who have clinically relevant bipolar symptoms that do not fulfill the DSM-IV criteria for BPI or BPII, but have a distinct period of abnormally elevated, expansive, or irritable mood plus the following:
1. Two DSM-IV manic symptoms or three DSM-IV manic symptoms if the mood is irritable clearly associated with the onset of abnormal mood
2. A clear change in the level of functioning
3. Mood and symptom duration of a minimum of 4 hours within a 24 hour period
4. A minimum of 4 days meeting the mood, symptom, duration, and functional change criteria over the subject's lifetime

Table 2. Demographic Information for Bipolar I versus Bipolar NOS Patients in Pediatric Bipolar Clinic

		Bipolar Status		
Characteristic	Bipolar Population (N = 68)	Bipolar I (n = 29)	Bipolar NOS (n = 39)	Test Statistic and *p*-value
Age in years, M (SD)	12.3 (2.9)	13.7 (2.3)	11.3 (2.9)	$t = 3.55$, $p < .0007$
Gender, n (%)				Fisher's exact test, $p < .20$
Male	42 (61.8)	15 (51.7)	27 (69.2)	
Female	26 (38.2)	14 (48.3)	12 (30.8)	
Ethnicity, n (%)				Fisher's exact test, $p < .21$
Caucasian	53 (77.9)	24 (82.8)	29 (74.4)	
African American	10 (14.7)	2 (7.0)	8 (20.5)	
Hispanic	1 (1.5)	1 (3.4)	0 (0.0)	
Asian	1 (1.5)	1 (3.4)	0 (0.0)	
Other	3 (4.4)	1 (3.4)	2 (5.1)	
Family Psychiatric History, n (%)				
Bipolar Disorder	45 (66.2)	22 (75.8)	23 (58.9)	Fisher's exact test, $p < .38$
Depression	41 (60.3)	19 (65.5)	22 (56.4)	Fisher's exact test, $p < .85$
Substance Abuse	25 (36.7)	10 (34.5)	15 (38.4)	Fisher's exact test, $p < .92$
Comorbid Psychiatric Disorders, n (%)				
ADHD	28 (41.2)	8 (27.6)	20 (51.3)	Fisher's exact test, $p < .08$
ODD	6 (8.8)	3 (10.3)	3 (7.7)	Fisher's exact test, $p < .99$

Note. The means (M) presented in this table are the sample means; SD = Standard Deviation.

weightings for each symptom using a 0 to 3 value of intensity (Gullion & Rush, 1998; Trivedi et al, 2004). The total test score ranges from 0-27.Threshold scores for depression were established as follows: 0-5 (not depressed); 6-10 (mild depression); 11-15 (moderate depression); 16-20 (severe depression); 21-27 (very severe depression). The PBD clinic developed a three point, Likert-type scale to assess the frequency of overt verbal and physical aggression over the past week. The scale is scored from 0-3; 0 being no aggression; 1 being aggressive behaviors present for 1-2 days; 2 being aggressive behaviors present for 3-4 days and 3 being aggressive behaviors present for 5-7 days over the past week. The diagnosis of Attention-Deficit Hyperactivity Disorder (ADHD) was established using the DSM-IV-TR criteria. A parent rated ADHD symptom scale (DuPaul, Power, Anastopoulos, & Reid, 1998) assessed the frequency of ADHD symptoms in the bipolar child/adolescent over the past week. There are 18 items on this scale and it is scored as follows: 0= Never or rarely; 1=sometimes; 2=often; 3=very often. The Clinical Global Impression - Severity (CGI-S; National Institute of Mental Health, 1976) scale was used to assess severity of overall functioning. This scale is scored as follows: 0=not assessed; 1=normal, not at all ill; 2=borderline mentally ill; 3=mildly ill; 4=moderately ill; 5=markedly ill; 6=severely ill and 7=among the most extremely ill patients.

Prior exposure to psychotropic medications, comorbidity, with bipolar disorder and family psychiatric history were also assessed. Family psychiatric history was assessed by direct questioning of the family members.

Data Analysis

Descriptive statistics were reported for the demographics and for the baseline clinical characteristics. For the comparative analyses, bipolar patients were divided into two groups: BPI and BPNOS. Two-independent sample *t*-test, with the Satterthwaite method for unequal variances (for continuous outcomes) and Fisher's Exact test (for categorical outcomes) were used to compare the two Bipolar groups (BPI vs. BPNOS) on the various demographics and baseline clinical characteristics. The level of significance was set at $\alpha = 0.05$.

Results

Demographic and Baseline Clinical Characteristics of Bipolar Youth

Demographic and baseline clinical characteristics (N=68) are shown in Tables 2 and 3, respectively. Of the 68 youth who entered the Bipolar clinic, about 77.9% were Caucasian, 61.8% were male, and the mean age was 12.3 years (*SD*=2.9). Twenty-nine youth (42.6%) were diagnosed as having BPI disorder (mean age: 13.7,

Table 3. Baseline Psychometric Data for BD I versus BPNOS Patients in Pediatric Bipolar Clinic

Test	Bipolar Diagnoses: Bipolar I (n = 29)	Bipolar Diagnoses: Bipolar NOS (n = 39)	Test Statistic[a] and *p*-value
YMRS Total, M (SD)	20.1 (11.2)	15.0 (7.7)	$t = 2.06$, $p < .04$
Elevated Mood:			
YMRS Item 1, M (SD)	1.4 (1.4)	0.9 (1.0)	$t = 1.79$, $p < .08$
Increased Motor Activity- Energy:			
YMRS Item 2, M (SD)	1.7 (1.2)	1.3 (1.1)	$t = 1.43$, $p < .15$
Sexual Interest:			
YMRS Item 3, M (SD)	0.7 (1.1)	0.5 (1.0)	$t = 0.75$, $p < .45$
Sleep: YMRS Item 4, M (SD)	1.4 (1.2)	0.9 (1.1)	$t = 1.91$, $p < .06$
Irritability: YMRS Item 5, M (SD)	3.1 (1.9)	2.9 (1.6)	$t = 0.28$, $p < .78$
Speech: YMRS Item 6, M (SD)	2.8 (2.4)	1.6 (1.4)	$t = 2.30$, $p < .02$
Language: Thought Disorder:			
YMRS Item 7, M (SD)	1.5 (1.1)	0.83 (0.95)	$t = 2.41$, $p < .02$
Thought Content:			
YMRS Item 8, M (SD)	2.8 (2.6)	1.5 (2.1)	$t = 2.18$, $p < .03$
Disruptive–Aggressive behavior:			
YMRS Item 9, M (SD)	2.5 (1.8)	2.7 (1.9)	$t = 0.48$, $p < .63$
Appearance:			
YMRS Item 10, M (SD)	0.7 (1.0)	0.5 (0.9)	$t = 0.74$, $p < .46$
Insight: YMRS Item 11, M (SD)	1.4 (1.0)	1.2 (1.1)	$t = 0.70$, $p < .48$
QIDS-A-SR Parent Total, M (SD)	11.6 (4.9)	10.1 (3.5)	$t = 1.36$, $p < .18$
Physical Aggression Score, M (SD)	1.2 (1.0)	1.1 (1.0)	$t = 0.50$, $p < .62$
Verbal Aggression Score, M (SD)	1.8 (1.2)	1.7 (0.9)	$t = 0.53$, $p < .59$
ADHD Checklist Total, M (SD)	23.0 (15.0)	35.1 (14.9)	$t = 1.65$, $p < .10$
CGI-S Total, M (SD)	4.5 (1.2)	4.3 (0.77)	$t = 0.83$, $p < .41$

Note. The means (M) presented in this table are the sample means; SD = Standard Deviation; YMRS = Young Mania Rating Scale; CGI-S = Clinical Global Impression - Severity; QIDS-A-SR = Quick Inventory of Depressive Symptomatology - Adolescent Version - Self-Report. [a]Tested for differences between Bipolar I and Bipolar NOS on each clinical characteristic in a separate model.

SD= 2.3 years) and 39 (57.4%) were diagnosed as having BPNOS (mean age: 11.3, SD= 2.9 years). As expected, many youth had a comorbid diagnosis of ADHD and this was more common among those with BPNOS (51.3%) than BPI (27.6%), although this did not reach statistical significance.

Of the BPI youth 75.8 % had a family history of bipolar disorder, and 65.5 % had a family history of depression. These rates were slightly higher than in those with BPNOS (58.9% and 56.4%, respectively). 34.5% of the BPI youth and 38.4% of the BPNOS youth had a family history of substance abuse.

Baseline Mood Symptoms and Psychiatric Medications

We evaluated the mood state of each BPI youth at the initial visit based on the DSM-IV-TR criteria. The findings suggest that of the 29 BPI youth 6.9% (n=2) presented as

Table 4. Prior Exposure to Psychiatric Medications for Patients in Pediatric Bipolar Clinic

Type of Psychotropic	Bipolar I (n = 29)	Bipolar NOS (n = 39)
Mood Stabilizers[a], n (%)	12 (41.38)	13 (33.33)
Atypical Antipsychotics[b], n (%)	13 (44.83)	23 (58.97)
Stimulants[c], n (%)	9 (31.03)	19 (48.72)
Antidepressants[d], n (%)	9 (31.03)	14 (35.90)
Strattera, n (%)	5 (17.24)	4 (10.26)
Clonidine, n (%)	5 (17.24)	7 (17.95)

Note. [a]Mood stabilizers include lithium, divalproex sodium, carbamazepine, lamotrigine, and oxcarbazepine. [b]Atypical antipsychotics include risperidone, quetiapine, aripiprazole, ziprasidone, and olanzapine. [c]Stimulants include methylphenidate, lisdexamfetamine, and amphetamine salts. [d]Antidepressants include bupropion, fluoxetine, duloxetine, citalopram, escitalopram, sertraline, venlafaxine, and paroxetine.

being manic, 34.5% (n=10) as being hypomanic, 10.3% (n=3) as being depressed, 41.4% (n=12) presented as being mixed, and 6.9% presented (n=2) in an unspecified mood state.

Table 3 presents symptom presentation for both bipolar groups. Overall, global severity in both groups was moderate. However, examination of the mania symptoms using the YMRS showed that the BPI group was significantly more severe than the BPNOS group (20.0, SD=11.2 vs. 15.0, SD=7.7; $p<.04$). Within individual YMRS items, only on Speech ($p<.02$), Thought Disorder ($p<.02$) and Thought Content ($p<.03$) were significantly greater in the BPI group compared to the BPNOS.

Discussion

Many children and adolescents in the community do not fit the classic DSM-IV-TR criteria for BPI, often making BPNOS the "catch all" diagnosis. Although previous research has been conducted to better understand the phenomenology of the spectrum of bipolar disorder, there are presently different operational definitions for bipolar disorder, in both clinical and research settings. The COBY study has not only provided research definitions for BPNOS but also provided preliminary validation for this diagnosis.

It is important to recognize that manic symptoms are the same in BPI and BPNOS, although the severity and duration of symptoms may differ. Thus, when youth present with symptoms of elevated mood, hypersexuality, decreased need for sleep, flight of ideas and/or grandiosity, a diagnosis within the bipolar spectrum disorders is likely to be present. However, distinguishing between BPI and BPNOS can be made by examining the severity and duration of symptoms. For example, in this study of a clinic sample, BPI youth had more severe manic symptoms, which was consistent with the findings in the COBY study (Axelson et al., 2006). It is important to ask about family history in youth with bipolar spectrum disorders, as children and adolescents diagnosed with either BPI or BPNOS both have strong family psychiatric histories.

Contrary to the classic manic symptoms described above, many youth will present to pediatricians, primary care physicians, and psychiatrists with irritability, emotional reactivity, distractibility and hyperactivity -all of which can be present in other psychiatric disorders such as ADHD, ODD, conduct disorder, post-traumatic stress disorder and pervasive developmental disorders (McClellan, 2007). Without specific guidelines for diagnosing the bipolar spectrum disorders, it is easy to misdiagnose and overdiagnose the bipolar spectrum disorders. At present, the COBY criteria appear to be the most clearly identified, and therefore it seems clinically befitting to apply such criteria for BPNOS into a clinical setting. Also, the use of stringent criteria for diagnosing the bipolar spectrum disorders forces one to make careful differential diagnoses of psychiatric conditions. It is clinically relevant to note that both bipolar groups are equally likely to have similar prior exposure to psychotropic medications, indicating significant interventions for treatment of their symptoms. In fact, it was noted that the BPNOS youth had had more prior exposure during their lifetime to atypical antipsychotics, stimulants and antidepressants than the BPI youth (Table 4). This finding is important because it brings forth the difficulty in accurately diagnosing the bipolar spectrum disorders which, in turn drives treatment decisions.

While one limitation of the present study is that diagnosis of bipolar spectrum disorders was made by direct clinical interview, and not by standardized research instruments, this study still demonstrates that research diagnostic criteria may be effectively utilized in a clinical setting. Another limitation of this study is that this is a retrospective chart review. As such, we could have incomplete documentation of notes, difficulty interpreting information and problems in verifying information.

In conclusion, BPNOS is a serious chronic illness the diagnostic guidelines for which are still debatable. Until further clarification of this diagnosis, the COBY research definitions for BPNOS can be implemented into a clinical setting, and may serve to improve the precision of such diagnosis and thus future treatment outcomes.

Acknowledgements/Conflict of Interest

The authors have no financial relationships or conflicts to disclose.

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