ELSEVIER

Journal of Affective Disorders xx (2006) xxx–xxx

JOURNAL OF AFFECTIVE DISORDERS

www.elsevier.com/locate/jad

Preliminary communication

# The child bipolar questionnaire: A dimensional approach to screening for pediatric bipolar disorder

Demitri Papolos *, John Hennen, Melissa S. Cockerham, Henry C. Thode Jr., Eric A. Youngstrom

*The Juvenile Bipolar Research Foundation, United States*

Received 21 November 2005; received in revised form 16 March 2006; accepted 29 March 2006

**Abstract**

*Background:* The Child Bipolar Questionnaire (CBQ) is a rapid screener with a Core Index subscale of symptom dimensions frequently reported in childhood-onset bipolar disorder (BD) and scoring algorithms for DSM-IV BD, with and without attention-deficit/hyperactivity disorder (ADHD), and the proposed Narrow, Broad, and Core phenotypes. This report provides preliminary data on the reliability and validity of the CBQ.
*Method:* Test–retest and inter-rater reliability of the CBQ were assessed. The ability of CBQ screening diagnoses and of the CBQ Core Index subscale to effectively predict diagnostic classification by structured interview was assessed using the K-SADS P/L.
*Results:* Preliminary test–retest data showed excellent reliability for both the CBQ total score ($r=0.82$) and the Core Index subscale ($r=0.86$). Preliminary validity data was also promising. CBQ screening algorithms performed with a specificity of 97% and a sensitivity of 76% in classifying subjects with K-SADS P/L diagnosis of BD vs. no BD. The Core Index subscale had excellent agreement with K-SADS P/L diagnosis ($k=0.84$) in classifying BD, ADHD-only, and no diagnosis and demonstrated 100% sensitivity and 86% specificity in classifying BD vs. no BD.
*Limitations:* This preliminary data is from a sample enriched with bipolar disorder cases. Further validation is needed with samples in which childhood-onset BD is rarer and diagnoses more diverse.
*Conclusions:* The CBQ shows potential for rapid and economically feasible identification of possible childhood-onset BD cases as defined by DSM-IV criteria as well as by alternate disease phenotypes. Further validation studies will focus on inpatient and outpatient samples with a broader range of variability.


*Keywords:* Bipolar disorder; Childhood-onset; Rating scale; Child bipolar questionnaire; Screening; Reliability; Validity

## 1. Introduction

Although sharing some of the clinical features of adult-onset bipolar disorder (BD), childhood-onset BD often differs in duration and symptom quality from the adult criteria delineated in the American Psychiatric Association's (1994) Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (Faedda et al., 1995). In response to studies of childhood-onset BD that observed numerous, brief episodes of elated or irritable mood lasting hours to days (Geller et al., 2000; Papolos et al., 1996; Findling et al., 2002; Geller et al., 2004) or long sustained irritability without episodes (Wozniak et al., 1995; Carlson, 1998; Carlson and Kelly, 1998; Biederman et al., 2000a; Biederman et al.,

* Corresponding author.
*E-mail address:* dpapolos@jbrf.org (D. Papolos).

0165-0327/$ - see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.jad.2006.03.026

2000b), Leibenluft et al. (2003) proposed the "Narrow" phenotype, delineating a presentation similar to adult-onset mania with elated mood required, and the "Broad" phenotype, delineating chronic mood disturbance without elated mood. Another phenotypic alternative characterized by abrupt changes in mood, difficulty regulating aggression, intense fearfulness, and deficits in mobilization of arousal and sustained attention has also been proposed (Papolos and Papolos, 2001; Papolos et al., 2005b) (see Table 1 for phenotype definitions).

Thus far, these promising new ideas have not been incorporated into new rapid screening instruments for childhood-onset BD. An economically feasible screening instrument that identifies cases that potentially meet alternate phenotype criteria as well as DSM-IV criteria may be of great value in etiological and phenomenological research on BD in children. For clinicians, a rapid screening instrument that assesses not only the symptoms of mania but also multiple clinical dimensions commonly considered comorbid with BD in children may be of great value in facing the diagnostic challenge of parsing the overlapping symptom criteria of several childhood disorders (Papolos, 2003). The Child Bipolar Questionnaire was developed to meet these research and clinical objectives. We present early data on its reliability and validity in this report.

The 'gold standard' for research diagnosis has been the semi-structured diagnostic interview; for children this is most often the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) (Puig-Antich and Ryan, 1986). The K-SADS has been modified to include items specific to prepubertal mania, rapid cycling, ADHD, and both present and lifetime diagnosis (Kaufman et al., 1997; Geller et al., 2001). Further modifications have since been proposed to include items pertaining to the Narrow and Broad alternate disease phenotypes (Leibenluft et al., 2003). However, the research diagnostic interview format is frequently time-consuming, expensive to implement, and thus infeasible for assessment purposes in many settings.

The psychiatric rating scale offers a potentially more efficient and economical screening alternative to the diagnostic interview. One of the most respected scales used to assess psychopathology in children and adolescents is the Child Behavior Checklist (CBCL) (Achenbach, 1991). The CBCL is an empirically-derived, well-validated, parent-completed 101 item checklist intended to measure extent of psychopathology in children in the age range of 4 to 18 years. In a recently-published meta-analysis, Mick et al. (2003) examined the response patterns on the CBCL in relation to its capacity to identify children with early-onset bipolar disorder. The Mick et al. meta-analysis found a "consistent pattern of elevations in inattention/hyperactivity, depression/anxiety, and aggression" in children with a recorded bipolar disorder diagnosis (Mick et al., 2003; p. 1026). More recent data confirms that a CBCL-Pediatric Bipolar Disorder (PBD) profile involving deviant findings on the Attention Problems, Aggressive Behavior, and Anxious-Depressed subscales effectively identifies current DSM-defined BD in children (Faraone et al., 2005). Although low scores on these subscales

Table 1
Proposed alternative phenotypes for childhood-onset BD

| Phenotype | Mood | Symptoms | Duration |
|---|---|---|---|
| DSM-IV | Elated and/or irritable | 3 or more (4 if irritable): grandiosity, decreased need for sleep, pressured speech, racing thoughts, distractibility, increase in activity, risky behavior | 1 week (or any duration if hospitalized) |
| Narrow | Must be elated | DSM-IV mania symptom criteria | 4 days |
| Broad | Angry, irritable; elation or grandiosity must *not* be present | Chronic irritability (marked reactivity to negative stimuli at least 3 times a week), baseline abnormal mood, chronic hyperarousal (distractibility, racing thoughts, pressured speech, intrusiveness, agitation, insomnia nearly everyday) | Chronic—no discernable episodes |
| Core | Elated and/or irritable | DSM-IV mania symptom criteria plus episodic and abrupt mood changes, poor modulation of aggressive, sexual, appetitive, or acquisitive drive (aggressive to self/others, hypersexual, relentlessly demanding) and four of the following: poor frustration tolerance, poor self-esteem regulation, sleep disturbances, excessive anxiety or fearfulness, oversensitivity to sensory stimuli, executive function deficits, family history of bipolar disorder | No duration required for manic episode; overall disturbance must continue for at least 12 months |

make it extremely unlikely that a child has BD, high scores are ambiguous because they indicate increased risk of both BD and various other conditions in which these symptoms also occur. Nonetheless, the CBCL studies suggest dimensions of illness in addition to mania that may be of considerable value in the assessment of childhood-onset BD. If demonstrated to be reliable and valid, a bipolar screening index derived from items that represent such dimensions could be a highly useful diagnostic tool, especially if derived from a brief instrument.

Brief screening instruments for childhood-onset BD include the Parent General Behavior Inventory (P-GBI) (Kahana et al., 2003), the Parent Young Mania Rating Scale (P-YMRS) (Gracious et al., 2002), and the Child Bipolar Questionnaire (CBQ). The P-GBI is adapted from the GBI to assess children's mood disorder symptoms. Parent responses identify mood states of even modest severity with specificity and sensitivity in children and adolescents (Findling et al., 2002; Youngstrom et al., 2001). A 10-item short form of the P-GBI has been developed using Receiver Operating Characteristic (ROC) analyses to identify the items with maximum discriminating power (Danielson et al., 2003). The P-YMRS is an 11-item Likert-scale instrument derived from the YMRS as a parent-report version. Both of these scales have performed well in psychometric studies, and, as Youngstrom et al. (2004) point out in their review of six potential screening instruments for bipolar disorder in children, "the P-YMRS and P-GBI produce fewer false alarms than the Achenbach scales do because high scores are more specific to youths with a bipolar diagnosis." The P-YMRS and the P-GBI focus entirely on manic and hypomanic content–e.g., elated mood, increased energy and activity, decreased sleep, racing thoughts and pressured speech, hypersexuality–and were not intended to diagnose alternate disease phenotypes, identify subtypes, or investigate dimensions of impairment associated with childhood-onset BD.

The Child Bipolar Questionnaire (CBQ) was developed as a self-administered, parent-report measure to establish initial eligibility for studies of childhood-onset bipolar disorder sponsored by the Juvenile Bipolar Research Foundation (JBRF). It was constructed based on the model proposed by Depue et al. (1981), who, with the development and validation of the General Behavior Inventory (GBI), derived a dimensional approach for the definition of bipolar disorder in adults. For the CBQ, 85 items were drawn from DSM-IV symptom criteria for mania, major depression, and common comorbid conditions: separation anxiety disorder, generalized anxiety disorder, obsessive–compulsive disorder, oppositional defiant disorder, conduct disorder, and attention-deficit disorder. Parents of a clinical sample of children diagnosed with bipolar disorder ($n=350$) were asked to rate the items on a Likert scale: "1" ("never"), "2" ("sometimes"), "3" ("often"), or "4" ("very often or almost constantly"). Those items rated "2" or higher by >70% of the parents were rank-ordered according to frequency of occurrence. Of these, the 65 highest ranked symptoms and behaviors were included in the final version of the CBQ.

Several screening algorithms have been derived from CBQ items in order to identify (1) possible BD cases as defined by DSM-IV and the Narrow, Broad, and Core phenotype symptom criteria, (2) possible BD cases with and without comorbid ADHD and (3) possible ADHD cases with no mood disorder. The CBQ total score, a count of all items rated "3" ("often") or "4" ("very often or almost constantly"), assesses severity of illness. The Core Index subscale, scored in the same manner, consists of 22 CBQ items determined through factor analytic methods in a separate study to represent prominent symptom dimensions of childhood-onset BD, including, but not limited to, manic symptoms. Clinical features relevant to the treatment of bipolar disorder such as suicidality, aggressive behavior, and psychosis are also assessed.

The CBQ has an estimated reading level of grade 8 and has been translated into Spanish, French, Polish, and Portuguese. It may be self-administered by a primary caretaker or completed by a clinician. Alone or in combination with other instruments, the CBQ may prove to be an effective screening tool for childhood-onset BD for both clinical and research purposes. In this report, we provide preliminary findings on the reliability and validity of the CBQ in a sample of children recruited via the JBRF data acquisition system.

## 2. Methods

### 2.1. Construction of CBQ diagnostic algorithms

In a prior study investigating the number of subjects in the larger JBRF database potentially meeting symptom criteria for each of the proposed alternate phenotypes for childhood-onset BD, screening algorithms were derived from CBQ items for the Narrow and Broad phenotypes (Leibenluft et al., 2003) and a Core phenotype proposed by the principal author (Papolos, in press) (see Table 2). To attain a degree of confidence about persistence of symptoms, the algorithms require that a symptom be rated "4—very often or almost constantly" to be counted as present.

Table 2
CBQ-derived screening algorithms

*Narrow phenotype = rated 4 on:* "Has elated or silly, goofy, giddy mood states" or "Has exaggerated ideas about self or abilities" *and three or more of the following:* (a) "Is hyperactive and easily excited in the PM" or "Has difficulty settling at night" or "Has difficulty getting to sleep"; (b) "Is easily distracted by extraneous stimuli" or "Is easily distracted during repetitive chores and lessons" or "Demonstrates inability to concentrate at school"; (c) "Has periods of high, frenetic energy and motor activation"; (d) "Has many ideas at once"; (e)"Interrupts or intrudes on others" or "Has periods of excessive and rapid speech"; (f) "Has exaggerated ideas about self or abilities"; (g) "Exhibits inappropriate sexual behaviors" or "Takes excessive risks".

*Broad Phenotype = rated 4 on:* "Has irritable mood states" *and must not be rated ≥ 2 on* "Has exaggerated ideas about self or abilities" and "Has elated or silly, goofy, giddy mood states." *In addition, one or more of the following:* "Has protracted, explosive temper tantrums," "Displays aggressive behavior towards others," "Has destroyed property intentionally," "Curses viciously, uses foul language in anger," "Makes moderate threats to others or self," "Makes clear threats of violence to others or self" and *three or more of the following:* (a) "Has difficulty settling at night" or "Has difficulty getting to sleep" or "Sleeps fitfully and/or awakens in the middle of the night" or "Has night terrors and/or nightmares"; (b) "Is easily distracted by extraneous stimuli" or "Is easily distracted during repetitive chores and lessons" or "Demonstrates inability to concentrate at school" or "Attempts to avoid homework assignments" or "Able to focus intently on subjects of interest and yet at times is easily distractible"; (c) "Is easily excitable" or "has periods of high, frenetic energy and motor activation" or "fidgets with hands"; (d) "Has many ideas at once"; (e) "Interrupts or intrudes on others"; (f) "Has periods of excessive and rapid speech".

*Core phenotype = DSM-IV Bipolar Disorder criteria are met (see below) and one of the following must be rated 4:* (a) "Craves sweet-tasting foods" or "Relentlessly pursues own needs and is demanding of others" or "Hoards or avidly seeks to collect objects or food"; (b) "Is bossy towards others" or "Displays aggressive behavior towards others" or "Has destroyed property intentionally" or "Curses viciously, uses foul language in anger" or "Makes moderate threats to others or self" or "Makes clear threats of violence to others or self" or "Is fascinated with gore, blood, or violent imagery"; (c) "Displays precocious sexual curiosity" or "Exhibits inappropriate sexual behaviors"; *in addition, four or more of the following must be rated 4:* (a) "Displays excessive distress when separated from family" or "Exhibits excessive anxiety or worry" or "Has concern with dirt, germs, or contamination"; (b) "Is easily distracted by extraneous stimuli" or "Is easily distracted during repetitive chores and lessons" or "Demonstrates inability to concentrate at school" or "Attempts to avoid homework assignments" or "Able to focus intently on subjects of interest and yet at times is easily distractible"; (c) "Attempts to avoid homework assignments" or "Has poor handwriting" or "Has difficulty organizing tasks" or "Has difficulty making transitions" or "Has difficulty estimating time" or "Has auditory processing or short-term memory deficit"; (d) "Is intolerant of delays" or "Defies or refuses to comply with rules" or "Is easily angered in response to limit setting" or "Has protracted explosive temper tantrums"; (e) "Has exaggerated ideas about self or abilities" or "Has decreased initiative" or "Experiences periods of self doubt and poor self-esteem" or "Feels easily criticized and/or rejected" or "Feels easily humiliated or shamed"; (f) "Has acknowledged experiencing auditory and/or visual hallucinations; (g) "Is extremely sensitive to textures of clothes, labels, and tightness of fit of socks or shoes" or "Exhibits extreme sensitivity to sound and noise" or "Complains of body temperature extremes or feeling hot despite neutral ambient temperature"; (h) "Has difficulty arising in the AM" or "Has difficulty settling at night" or "Has difficulty getting to sleep" or "Sleeps fitfully and/or awakens in the middle of the night" or "Has night terrors and/or nightmares" or "Wets bed"; (i) "Is easily excitable" or "Is willful and refuses to be subordinated by others" or "Blames others for his/her mistakes" or "Is easily angered in response to limit setting" or "lies to avoid consequences of his/her actions".

*DSM-IV Bipolar Disorder (inclusive of BPI, BPII, and BP-NOS) = rated ≥ 3 on one or more:* "Displays abrupt, rapid mood swings", "Has irritable mood states", "Has elated or silly, goofy, giddy mood states" *and on four or more of the following:* (a) "Is hyperactive and easily excited in the PM" or "Has difficulty settling at night" or "Has difficulty getting to sleep"; (b) "Has periods of high, frenetic energy and motor activation"; (c) "Has many ideas at once"; (d) "Interrupts or intrudes on others" or "Has periods of excessive and rapid speech"; (e) "Has exaggerated ideas about self or abilities"; (f) "Exhibits inappropriate sexual behaviors" or "Takes excessive risks".

*DSM-IV Bipolar Disorder with ADHD = Bipolar Disorder criteria are met and must score ≥ 3 on three or more*: "Is easily distracted by extraneous stimuli" or "Is easily distracted during repetitive chores and lessons" or "Demonstrates inability to concentrate at school" or "Attempts to avoid homework assignments" or "Able to focus intently on subjects of interest and yet at times is easily distractible" or "Has poor handwriting" or "Has difficulty organizing tasks" or "Has difficulty making transitions" or "Has difficulty estimating time".

*ADHD-only = Must score ≥ 3 on three or more:* (a) "Is easily distracted by extraneous stimuli" or "Is easily distracted during repetitive chores and lessons" or "Demonstrates inability to concentrate at school" or "Attempts to avoid homework assignments" or "Able to focus intently on subjects of interest and yet at times is easily distractible" or "Has poor handwriting" or "Has difficulty organizing tasks" or "Has difficulty making transitions" or "Has difficulty estimating time." *Must not score ≥ 3 on more than three:* (a) "Is hyperactive and easily excited in the PM" or "Has difficulty settling at night" or "Has difficulty getting to sleep"; (b) "Has periods of high, frenetic energy and motor activation"; (c) "Has many ideas at once"; (d) "Interrupts or intrudes on others" or "Has periods of excessive and rapid speech"; (e) "Has exaggerated ideas about self or abilities"; (f) "Exhibits inappropriate sexual behaviors" or "Takes excessive risks".

### 2.2. Construction of the CBQ Core Index subscale

In a separate prior study, a series of principal component factor analyses with Varimax rotation were carried out on CBQ data from a large subsample of the JBRF data set ($n = 2795$) to test a hypothesis concerning

the core symptom dimensions of childhood-onset BD (Papolos, in press). The CBQ items loading on the resulting factors comprise the Core Index subscale (see Table 3).

### 2.3. Sample

Since June 2000, parents or primary caretakers have participated in an online research program on a secure domain of the JBRF website, providing data on 5120 children and adolescents, aged 5–17. Of these, 3430 (66.9%) have been assigned the diagnosis of bipolar disorder by a clinician (child psychiatrist, psychiatrist, psychologist, pediatrician, or neurologist). The participants in the research program are a self-selected sample, referred to JBRF through national advocacy sites, online newsletters, and professionals who treat children with bipolar disorder. Informed consent must be given before parents may enter data using JBRF's interactive data acquisition program. Data are stored using unique confidential parent and child ID numbers. The JBRF uses the Child Bipolar Questionnaire to determine potential eligibility for research studies and maintains email contact with the parents who submit this data to inform them of their children's initial eligibility.

Table 3
CBQ Core Index subscale

| |
|---|
| (1) Displays excessive distress when separated from family |
| (2) Exhibits excessive anxiety or worry |
| (6) Has difficulty getting to sleep |
| (8) Has night terrors and/or nightmares |
| (10) Craves sweet-tasting foods |
| (23) Complains of body temperature extremes or feeling hot despite neutral ambient temperature |
| (26) Has many ideas at once |
| (27) Interrupts or intrudes on others |
| (31) Displays abrupt, rapid mood swings |
| (32) Has irritable mood states |
| (33) Has elated or silly, goofy, giddy mood states |
| (36) Takes excessive risks |
| (38) Has periods of low energy and/or withdraws or isolates self |
| (39) Has decreased initiative |
| (40) Experiences periods of self doubt and poor self-esteem |
| (42) Feels easily humiliated or shamed |
| (52) Lies to avoid consequences of his/her actions |
| (53) Has protracted, explosive temper tantrums |
| (55) Displays aggressive behavior towards others |
| (62) Has acknowledged experiencing auditory and/or visual hallucinations |
| (63) Hoards or avidly seeks to collect objects or food |
| (64) Has concern with dirt, germs, or contamination |

### 2.4. Reliability assessment procedures

Reliability assessment included three different methods: internal consistency assessment, test–retest agreement, and inter-rater (virtually always, inter-parent) concordance. The internal consistency estimation was performed on a large CBQ data set ($n=2427$) using Cronbach's alpha procedure. The test–retest procedure was conducted by requesting via email that the first 100 consecutive parents submitting CBQ data over the course of 3 months repeat their ratings within 7 days of their initial ratings. In this manner, test–retest data was collected on 108 children. The inter-rater reliability assessment was conducted similarly, with 50 consecutive parents requested to ask another parent or close family member to separately rate their child/adolescent within 7 days of each other. Inter-rater reliability data was collected on 48 children in this manner. Reliability of the CBQ total score, the CBQ Core Index subscale, and the CBQ-based screening algorithms was assessed.

### 2.5. Validity assessment procedures

A subsample of children from the larger data set were recruited for participation in JBRF-sponsored studies of childhood-onset BD, including a neuropsychological testing study of BD and ADHD-only group differences and a genetic linkage study of sibling pairs with BD. Children without psychiatric disturbance were also recruited for comparison purposes. Eligibility for these studies required diagnostic confirmation via administration of the K-SADS P/L diagnostic interview to both parent and child. Parents and 135 children were interviewed by four graduate-level interviewers trained in the administration of the K-SADS P/L by the JBRF project director, who had been approved after training with Dr. Joan Kaufman. Three diagnostic groups were represented in the sample: BD (inclusive of BP I, BP II, and BP-NOS), ADHD-only, and no psychiatric diagnosis. Construct validity was assessed by comparing CBQ-based screening diagnosis with K-SADS P/L-based diagnosis. In addition, the CBQ Core Index subscale was assessed for its ability to predict membership in the three diagnostic groups.

Parents of a separate subsample of 497 children from the larger data set, 325 of whom had a community diagnosis of bipolar disorder, provided additional experiential and behavioral histories, such as prior psychiatric hospitalizations, school difficulties, and involvement with the juvenile justice system. Concurrent validity was examined in this sample to determine whether CBQ total score differed among subgroups with differential experiences.

## 3. Results

### 3.1. Reliability measures

#### 3.1.1. Internal consistency

Cronbach [alpha] coefficient was calculated to evaluate the internal consistency of the CBQ. In subjects reported by their parents to have a clinician-assigned diagnosis of bipolar disorder, the alpha estimate for the CBQ was 0.929 ($n=2427$).

#### 3.1.2. Test–retest reliability

The average time between CBQ test and retest was 3 days. Reliability of the CBQ total score and the CBQ Core Index score was assessed using a Pearson's correlation between the first and second rating for each subject. The correlations between the test and retest values of the CBQ total score and the CBQ Core Index subscale were 0.82 and 0.86 respectively. Both are considered in excellent agreement (Fleiss, 1981). Reliability of the CBQ screening algorithms was assessed by comparing the diagnosis indicated by the first rating for each subject to that indicated by the second rating using a kappa coefficient. In this comparison three classifications were used: BD (DSM-IV phenotype), ADHD-only, and neither psychiatric diagnosis (see Table 2 for screening algorithms). Based on the first rating, 85 (79%) were classified as BD, 19 subjects (18%) were classified as ADHD, and 4 subjects (4%) were classified as having neither diagnosis. Within diagnostic group, the test–retest concordance estimates were 0.81 for BD, 0.74 for ADHD, and 0.76 for neither diagnosis, all considered in excellent agreement.

#### 3.1.3. Inter-rater (inter-parent) reliability

Each of 48 subjects was rated once by each of two different raters using the CBQ. In all cases, the first responder was the mother of the child while the second responder was most often the father (79%). Reliability of the CBQ total score and the CBQ Core Index score was assessed using a Pearson's correlation between the first and second rating for each subject. The correlations between the first and second values of the CBQ total score and the Core Index score were 0.54 and 0.52 respectively, considered fair to good agreement (Fleiss, 1981). Reliability of the CBQ screening algorithms was assessed by comparing the diagnosis indicated by the first rating to that indicated by the second rating using a kappa coefficient. The correlations within diagnostic group were similar to that for the full set of subjects: for the ADHD subjects ($n=12$) the correlation was 0.54, and for the BD subjects ($n=35$) the correlation was 0.53. These findings are comparable to the typical levels of inter-rater agreement between adults describing a child's behavior in the same setting (Achenbach et al., 1987).

### 3.2. Construct validity

#### 3.2.1. CBQ screening algorithms

Using the KSADS P/L, 76 subjects (56%) were diagnosed with BD (DSM-IV phenotype), 21 subjects (16%) with ADHD without mood disorder, and 38 subjects (28%) with no psychiatric diagnosis. Of the 76 subjects diagnosed with BD, 26 were diagnosed with Bipolar I Disorder, 5 with Bipolar II Disorder, and 45 with Bipolar Disorder, Not Otherwise Specified (BP-NOS). Those diagnosed with BP-NOS had manic symptoms of briefer duration than required by DSM-IV; the majority of these had rapid alternation of mood states within the same day. The CBQ screening algorithm for BD (DSM-IV phenotype) correctly classified 57 of 59 subjects who did not have BD (specificity=97%) and 58 of 76 subjects who had BD (sensitivity=76%), yielding an overall kappa of 0.71. Using the CBQ screening algorithms to differentiate between three diagnostic groups, there was an overall kappa of 0.69 (fair to good agreement) with an overall rate of agreement of 81%. The CBQ screening algorithm correctly classified all but 1 of the subjects with no psychiatric diagnosis (97% correct screening). Fourteen of the 21 ADHD subjects (67%) were correctly classified, and 58 of the 76 BD subjects were correctly classified (76%).

#### 3.2.2. Validity of the CBQ Core Index

To identify the differentiating power of the CBQ Core Index, a discriminant analysis was performed using the CBQ Core Index score as the only predictor variable. The dependent variable used in this analysis was the K-SADS diagnosis using the three groups: BD, ADHD, and no psychiatric diagnosis. From this analysis it was determined that if the CBQ Core Index subscale score was 0 or 1, a subject should be classified as having no diagnosis; 36 out of the 38 subjects (95%) were correctly classified. A subject with a CBQ Core Index score of 2 or 3 was predicted to have ADHD-only. Subjects with a score of 4 or higher were classified as BD. The kappa coefficient for agreement between the CBQ Core Index score with stated cut-offs and the K-SADS diagnosis was 0.84, indicating excellent agreement. After combining the normal and ADHD groups so that the analysis consisted of BD vs. no BD, the CBQ Core Index score with a cut-off of 4 had 100%

sensitivity, 86% specificity, 100% negative predictive value and 90% positive predictive value.

### 3.2.3. Using the CBQ to classify subjects into subgroups with and without comorbid ADHD

Of the 76 subjects diagnosed with BD using the K-SADS P/L, 51 were diagnosed with comorbid ADHD. The ability of the CBQ to differentiate those BD cases with ADHD from those without was explored using logistic regression. All 65 questions of the CBQ were candidates for predicting subgroup membership. Forward inclusion stepwise methods were used to identify those predictors that were statistically significant. All 65 items were entered into the stepwise analysis, and two items were identified as being statistically significant—item 11 ("is easily distracted by extraneous stimuli") and item 14 ("attempts to avoid homework assignments"). In simplified form, an algorithm for classifying subjects was proposed: if both item 11 and item 14 are rated 3 or higher, then BD with ADHD is indicated; if at most one of the items is rated 3 or higher, then BD without ADHD is indicated. This rule correctly identified 39 of the 51 BD subjects with ADHD (77%) and 17 of the 25 BD subjects without ADHD (68%).

### 3.2.4. Concurrent validity

Additional history data were obtained from the parents of a subsample of 497 subjects, 325 of whom had a community diagnosis of bipolar disorder. These supplemental data included information such as age of onset of psychiatric difficulties; current and first psychiatric diagnoses; whether or not there was a history of psychiatric hospitalization and, if so, how many inpatient stays; duration of periods of mood stability/instability, school difficulties (whether held back in school); and presence/absence of involvement with the juvenile justice system. We examined whether CBQ total score differed between subgroups created with these variables (Table 4). CBQ total score was much higher among subjects with a parent-reported primary diagnosis of bipolar disorder compared to all other diagnoses. This contrast was statistically significant. Similarly, children/adolescents reported to have had prior psychiatric hospitalizations had much higher scores, on average, on the CBQ than subjects who were reported not to have been hospitalized. Children with an early onset of psychiatric illness, dichotomized as onset ≤age 3 years vs. onset >3 years, had significantly higher scores on the CBQ. On two important indicators of functioning, school difficulties and involvement with the juvenile justice system, parents reported a high incidence of impairment, with fully 15% of parents acknowledging school problems and 11% reporting juvenile justice system problems. Among subjects reported by parents to have been held back at school at least 1 year, CBQ total scores were much higher than comparable CBQ scores for all other subjects in the subsample. Similarly, subjects reported by parents to have had at least one incident resulting in involvement with the juvenile justice system had much higher CBQ scores than other subjects.

Table 4
Associations of CBQ scores with selected psychiatric history events among 497 children/adolescents with supplemental questionnaire data

| History/event | *n* | CBQ Total |
|---|---|---|
| Primary diagnosis | 497 | |
| Bipolar disorder | 325 | 46.1 (8.6) |
| Other | 172 | 42.7 (10.1) |
| *z*-statistic[a] | | 3.67, $p<0.001$ |
| Hospitalizations, psych. | 497 | |
| One or more | 189 | 48.3 (8.9) |
| None | 308 | 42.8 (8.9) |
| *z*-statistic[a] | | 6.53, $p<0.001$ |
| Symptom onset | 497 | |
| Onset ≤3 years | 372 | 45.6 (9.2) |
| Onset >3 years | 125 | 42.8 (9.3) |
| *z*-statistic[a] | | 3.15, $p=0.002$ |
| School held-back | 455 | |
| At least one grade | 71 | 48.6 (9.1) |
| Never | 384 | 44.6 (9.1) |
| *z*-statistic[a] | | 3.34, $p=0.001$ |
| Juvenile justice contact | 497 | |
| One or more times | 57 | 48.4 (8.0) |
| Never | 440 | 44.5 (9.4) |
| *z*-statistic[a] | | 3.03, $p=0.003$ |

[a] *z*-statistic calculated using generalized linear modeling methods (Gaussian family), adjusting for age and sex, with robust estimation of standard errors.

## 4. Discussion

Some of the most difficult questions surrounding childhood-onset bipolar disorder have to do with phenomenological issues. There is, as yet, no consensus in the field on diagnostic criteria for the disorder as it presents in children, although alternate disease phenotypes have been proposed by several clinical investigators (Leibenluft et al., 2003; Geller et al., 2004; Papolos et al., 2005a). The boundaries between the BD syndrome and other psychiatric conditions of childhood remain in debate, although clinicians consider this crucial to appropriate therapeutic intervention (Sasson et al., 2003; Kowatch et al., 2005). The psychiatric rating scales heretofore available for rapid and cost-efficient administration in research and clinical settings continue to be based on DSM-IV criteria, although most

researchers agree that there are significant differences in adult and child presentation.

This report has presented preliminary psychometric data on the Child Bipolar Questionnaire, a 65 item parent-report rating scale that takes approximately 10 min to complete and lends itself easily to self-administration via the internet or to administration by a clinician. This screening instrument was originally designed as a research tool to rapidly identify potential BD cases for diagnostic confirmation and to assist in defining subgroups for genotyping. The CBQ-based scoring algorithms screen for those who may meet symptom criteria for DSM-IV mania and several alternate disease phenotypes. The Core Index subscale of the CBQ represents key symptom dimensions in childhood-onset BD that may be used to build homogeneous subgroups for study. Finally, CBQ item level data has been used to study factors associated with suicide threat and with poor regulation of aggressive behavior (Papolos et al., 2005a).

The CBQ demonstrated excellent test–retest reliability in this internet sample. Inter-rater reliability was only fair, consistent with reports about inter-rater agreement. Preliminary validation efforts show the CBQ to be effective in predicting the diagnostic classification of youth by structured clinical interview. In a sample in which the K-SADS P/L was used to confirm bipolar diagnosis, the CBQ screening algorithm for BD was able to identify 76% of subjects with a DSM-IV diagnosis of BD and performed very well at ruling out children with ADHD or no psychiatric diagnosis (97%). The CBQ Core Index, a subscale comprised of 22 items identified in prior study as representing prominent symptom dimensions of childhood-onset BD, demonstrated excellent reliability and performed very well in exploratory efforts to differentiate children with BD from those with ADHD-only. The CBQ screening algorithms, developed in prior study to identify candidates meeting symptom criteria for several disease phenotypes, performed surprisingly well in exploratory efforts to differentiate BD with ADHD from BD without ADHD. This very important distinction may be crucial in the identification of the boundaries of these syndromes: comorbid conditions with unique but possibly partially shared genetic diatheses, or members of a spectrum of conditions that share discrete symptoms.

Overall kappa estimates may have been adversely affected by two factors. First is the lack of fit of the DSM-IV mania-based screening algorithm with the clinical presentation of most of the children in the sample. Of the 76 children given a K-SADS P/L diagnoses of bipolar disorder, only 26 were diagnosed with BP I. The majority of the children, 45 subjects, were diagnosed with BP-NOS, a diagnosis that was recommended for these children by experts at the NIMH 2001 Roundtable on Prepubertal Bipolar Disorder in the absence of a more appropriate phenotype (NIMH, 2001). The CBQ Core Index subscale, a measure based on analysis of symptom dimensions, performed better than the BD and ADHD screening algorithms when compared to K-SADS diagnoses, with a kappa coefficient indicating excellent agreement. Another factor that may have affected kappa estimates was the attempt to classify children having ADHD (without comorbid mood disorder) using the CBQ-based algorithms. This attempt was not as successful as the effort to differentiate children with bipolar disorder from those without (inclusive of ADHD-only cases and those with no psychiatric disorder). The CBQ was not designed to diagnose ADHD per se, but to assist in the task of differentiating the two diagnoses.

### 4.1. Limitations and caveats

Sample limitations are clear. All CBQ data were volunteered by parents to determine their children's initial eligibility for participation in the JBRF research program. Their report may have been influenced by their desire for their children to participate. However, while this may affect CBQ total score and perhaps the DSM-IV mania algorithm, the proposed alternative phenotypes are generally unknown to parents and the CBQ Core Index subscale items are not easily identifiable. All participants in the validity study, both parents and children, were administered the K-SADS P/L to confirm their diagnostic eligibility for the neuropsychological testing study and the genetic study, as is the procedure for all JBRF-sponsored studies. However, this is a sample heavily enriched for bipolar disorder and is not representative of a clinic or community sample, in which childhood-onset BD is rarer. The positive predictive power, negative predictive power and kappa will all change in such samples. Similarly, the comparison group in this validity study was limited to youths with no diagnosis or youths with ADHD but no comorbid mood disorder. These groups have been used in phenomenological studies (Geller et al., 2004); however, they represent only a portion of the diagnoses that present at many clinical settings. For example, cases with oppositional defiant disorder, conduct disorder, and major depressive disorder were not included. These diagnoses can also be difficult to distinguish from BD in their own right (Bowring and Kovacs, 1992; Spencer et

al., 2001; Kim and Miklowitz, 2002), and inclusion of these cases can substantially reduce the diagnostic specificity of a test (as more non-BD cases score in the false positive range) (Youngstrom et al., 2005). Also, few cases in the sample were diagnosed with Bipolar II disorder or cyclothymia. These are bipolar spectrum diagnoses that can be more difficult to recognize clinically or with screening measures (Miller et al., 2004; Youngstrom et al., 2001). We are currently conducting further assessments of CBQ validity in a large, diverse clinic population and in an inpatient unit of a children's psychiatric hospital.

## 5. Conclusion

With, as yet, no agreed upon uniform diagnostic criteria for bipolar disorder in children, it is a great challenge to develop a brief diagnostic instrument for youth that meets the needs of both researchers and clinicians. The Child Bipolar Questionnaire shows promise as a rapid and economically feasible way to screen for potential candidates meeting criteria for DSM-IV mania and several proposed alternate phenotypes. If further validation efforts are successful, the CBQ may be used by the clinician to aid in the early detection of BD features, the parsing of symptom dimensions and the differentiation of comorbid conditions for treatment focus. It may be used by researchers to aid in the further definition of the disease phenotype and the formation of more homogeneous pediatric samples for study of the neurobiology of bipolar disorder. The CBQ is available online at http://jbrf.org/cbq/index.html. An online scoring program for the CBQ is in development that provides total score and Core Index subscale score with diagnostic implications and a breakdown of symptom dimensions.

## References

Achenbach, T.M., 1991. Integrative Guide for the 1991 CBCL/4-18, YSR, and TRF Profiles. University of Vermont, Department of Psychiatry, Burlington, VT.

Achenbach, T.M., McConaughy, S.H., Howell, C.T., 1987. Child/adolescent behavioral and emotional problems: implication of cross-informant correlations for situational specificity. Psychol. Bull. 101, 213–232.

American Psychiatric Association, 1994. Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV). American Psychiatric Association, Washington, DC.

Biederman, J., Faraone, S.V., Wozniak, J., Monuteaux, M.C., 2000a. Parsing the association between bipolar, conduct, and substance use disorders: a familial risk analysis. Biol. Psychiatry 48 (11), 1037–1044.

Biederman, J., Mick, E., Faraone, S.V., Spencer, T., Wilens, T.E., Wozniak, J., 2000b. Pediatric mania: a developmental subtype of bipolar disorder? Biol. Psychiatry 48 (6), 458–466.

Bowring, M.A., Kovacs, M., 1992. Difficulties in diagnosing manic disorders among children and adolescents. J. Am. Acad. Child Adolesc. Psych. 31, 611–614.

Carlson, G.A., 1998. Mania and ADHD: comorbidity or confusion. J. Affect. Disord. 51 (2), 177–187.

Carlson, G.A., Kelly, K.L., 1998. Manic symptoms in psychiatrically hospitalized children—what do they mean? J. Affect. Disord. 51, 123–135.

Danielson, C.K., Youngstrom, E.A., Findling, R.L., Calabrese, J.R., 2003. Discriminative validity of the general behavior inventory using youth report. J. Abnorm. Child Psychol. 31 (1), 29–39.

Depue, R., Slater, J., Wolfstetter-Kausch, H., Klein, D., Goplerud, E., Farr, D., 1981. A behavioral paradigm for identifying persons at risk for bipolar depressive disorders: a conceptual framework and five validation studies. J. Abnorm. Psychology 90, 381–437.

Faedda, G.L., Baldessarini, R.J., Suppes, T., Tondo, L., Becker, I., Lipschitz, D., 1995. Pediatric-onset bipolar disorder: a neglected clinical and public health problem. Harv. Rev. Psychiatry 3 (4), 171–193.

Faraone, S.V., Althoff, R.R., Hudziak, J.J., Monuteaux, M., Biederman, J., 2005. The CBCL predicts DSM bipolar disorder in children: a receiver operating characteristic curve analysis. Bipolar Disord. 7 (6), 518–524 (Dec.).

Findling, R.L., Youngstrom, E.A., Danielson, C.K., DelPorto, D., Papish-David, R., Townsend, L., et al., 2002. Clinical decision-making using the General Behavior Inventory. Bipolar Disord. 4, 34–42.

Fleiss, J.L., 1981. Statistical Methods for Rates and Proportions. John Wiley and Sons, New York, NY.

Geller, B., Zimmerman, B., Williams, M., 2000. Diagnostic characteristics of 93 cases of prepubertal and early adolescent bipolar disorder phenotype by gender, puberty and comorbid attention deficit. J. Child Adolesc. Psychopharmacol. 10, 157–164.

Geller, B., Zimerman, B., Williams, M., Bolhofner, K., Craney, J.L., DelBello, M.P., Soutullo, C., 2001. Reliability of the Washington University in St Louis Kiddie Schedule for Affective Disorders and Schizophrenia (WASH-U-KSADS) mania and rapid cycling sections. J. Am. Acad. Child Adolesc. Psych. 40, 450–455.

Geller, B., Tillman, R., Craney, J.L., Bolhofner, K., 2004. Four-year prospective outcome and natural history of mania in children with a prepubertal and early adolescent bipolar disorder phenotype. Arch. Gen. Psychiatry 61, 459–467.

Gracious, B.L., Youngstrom, E.A., Findling, R.L., Calabrese, J.R., 2002. Discriminative validity of a parent version of the Young Mania Rating Scale. J. Am. Acad. Child Adolesc. Psych. 41, 1350–1359.

Kahana, S.Y., Youngstrom, E.A., Findling, R.L., Calabrese, J.R., 2003. Employing parent, teacher, and youth self-report checklists in identifying pediatric bipolar spectrum disorders: an examination of diagnostic accuracy and clinical utility. J. Child Adolesc. Psychopharmacol. 13, 471–488.

Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., Williamson, D., Ryan, N., 1997. Schedule for affective disorders and schizophrenia for school-age children—present and lifetime version (K-SADS-PL): initial reliability and validity data. J. Am. Acad. Child Adolesc. Psych. 36, 980–988.

Kim, E.Y., Miklowitz, D.J., 2002. Childhood mania, attention deficit hyperactivity disorder and conduct disorder: a critical review of diagnostic dilemmas. Bipolar Disord. 4, 215–225.

Kowatch, R.A., Fristad, M., Birmaher, B., Wagner, K.D., Findling, R. L., Hellander, M., Child Psychiatric Workgroup on Bipolar, D., 2005. Treatment guidelines for children and adolescents with bipolar disorder. J. Am. Acad. Child Adolesc. Psych. 44, 213–235.

Leibenluft, E., Charney, D.S., Towbin, K.E., Bhangoo, R.K., Pine, D. S., 2003. Defining clinical phenotypes of juvenile mania. Am. J. Psychiatry 160 (3), 430–437.

Mick, E., Biederman, J., Pandina, G., Faraone, S.V., 2003. A preliminary meta-analysis of the Child Behavior Checklist in pediatric bipolar disorder. Biol. Psychiatry 53, 1021–1027.

Miller, C.J., Klugman, J., Berv, D.A., Rosenquist, K.J., Ghaemi, S.N., 2004. Sensitivity and specificity of the Mood Disorder Questionnaire for detecting bipolar disorder. J. Affect. Disord. 81, 167–171.

National Institute of Mental Health: National Institute of Mental Health Research Roundtable on Prepubertal bipolar disorder, 2001. J. Am. Acad. Child Adolesc. Psych. 40, 871–878.

Papolos, D.F., 2003. Bipolar disorder and comorbid disorders: the case for a dimensional nosology. In: Geller, B., Delbello, M. (Eds.), Bipolar Disorder in Childhood and Early Adolescence. The Guilford Press, New York, NY.

Papolos, D.F., Papolos, J.D., 2001. The Bipolar Child: The Definitive and Reassuring Guide to One of Childhood's Most Misunderstood Disorders. Broadway Books, N.Y., New York.

Papolos, D.F., Hennen, J., Cockerham, M., 2005a. Factors associated with parent-reported suicide threats by children and adolescents with community-diagnosed bipolar disorder. J. Affect. Disord. 86 (2–3), 267–275.

Papolos, D.F., Hennen, J., Cockerham, M., 2005b. Obsessive fears about harm to self or others and overt aggressive behaviors in youth diagnosed with juvenile-onset bipolar disorder. J. Affect. Disord. 89 (1–3), 99–105.

Puig-Antich, J., Ryan, N., 1986. The Schedule for Affective Disorders and Schizophrenia for School-Age Children (Kiddie-SADS)-1986. Western Psychiatric Institute and Clinic, Pittsburgh, PA.

Sasson, Y., Chopra, M., Harrari, E., Amitai, K., Zohar, J., 2003. Bipolar comorbidity: from diagnostic dilemmas to therapeutic challenge. Int. J. Neuropsychopharmacol. 6 (2), 139–144.

Spencer, T.J., Biederman, J., Wozniak, J., Faraone, S.V., Wilens, T.E., Mick, E., 2001. Parsing pediatric bipolar disorder from its associated comorbidity with the disruptive behavior disorders. Biol. Psychiatry 49 (12), 1062–1070.

Wozniak, J., Biederman, J., Kiely, K., Ablon, J.S., Faraone, S.V., Mundy, E., Mennin, D., 1995. Mania-like symptoms suggestive of childhood-onset bipolar disorder in clinically referred children. J. Am. Acad. Child Adolesc. Psych. 34 (7), 867–876.

Youngstrom, E.A., Findling, R.L., Danielson, C.K., Calabrese, J.R., 2001. Discriminative validity of parent report of hypomanic and depressive symptoms on the General Behavior Inventory. Psychol. Assess. 13, 267–276.

Youngstrom, E.A., Findling, R.L., Calabrese, J.R., Gracious, B.L., Demeter, C., DelPorto Bedoya, D., Price, M., 2004. Comparing the diagnostic accuracy of six potential screening instruments for bipolar disorder in youths aged 5 to 17 years. J. Am. Acad. Child Adolesc. Psych. 43 (7), 847–858.

Youngstrom, E.A., Meyers, O.I., Demeter, C., Kogos Youngstrom, J., Morello, L., Piiparinen, R., 2005. Comparing diagnostic checklists for pediatric bipolar disorder in academic and community mental health settings. Bipolar Disord. 7 (6), 507–517.