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

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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.

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Although sharing some of the clinical features of adult bipolar disorder, childhood-onset bipolar disorder 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.,

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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., in press-b) (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-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 make it extremely

t1.1 Table 1
t1.2 Proposed alternative phenotypes for childhood-onset BD

t1.3	Phenotype	Mood	Symptoms	Duration
t1.4	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)
t1.5	Narrow	Must be elated	DSM-IV mania symptom criteria	4 days
t1.6	Broad	Angry, irritable; elation or grandiosity must <i>not</i> 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
t1.7	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

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 (Youngstrom, 2004). 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 PBD.

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 (Papolos et al., in press). 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.

t2.1 Table 2

t2.2 CBQ-derived screening algorithms

t2.3 *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”.

t2.5

t2.6 *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”.

t2.7

t2.8 *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

Table 2 (continued)

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”.

Occurrence of one or more items presented in parentheses is counted as one.

2.2. Construction of the CBQ Core Index subscale 230

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.

t3.1	Table 3
t3.2	CBQ Core Index subscale
t3.3	(1) Displays excessive distress when separated from family
t3.4	(2) Exhibits excessive anxiety or worry
t3.5	(6) Has difficulty getting to sleep
t3.6	(8) Has night terrors and/or nightmares
t3.7	(10) Craves sweet-tasting foods
t3.8	(23) Complains of body temperature extremes or feeling hot despite neutral ambient temperature
t3.9	(26) Has many ideas at once
t3.10	(27) Interrupts or intrudes on others
t3.11	(31) Displays abrupt, rapid mood swings
t3.12	(32) Has irritable mood states
t3.13	(33) Has elated or silly, goofy, giddy mood states
t3.14	(36) Takes excessive risks
t3.15	(38) Has periods of low energy and/or withdraws or isolates self
t3.16	(39) Has decreased initiative
t3.17	(40) Experiences periods of self doubt and poor self-esteem
t3.18	(42) Feels easily humiliated or shamed
t3.19	(52) Lies to avoid consequences of his/her actions
t3.20	(53) Has protracted, explosive temper tantrums
t3.21	(55) Displays aggressive behavior towards others
t3.22	(62) Has acknowledged experiencing auditory and/or visual hallucinations
t3.23	(63) Hoards or avidly seeks to collect objects or food
t3.24	(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 study. 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.

318 3. Results

319 3.1. Reliability measures

320 3.1.1. Internal consistency

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

326 3.1.2. Test–retest reliability

327 The average time between CBQ test and retest was
328 3 days. Reliability of the CBQ total score and the CBQ
329 Core Index score was assessed using a Pearson's
330 correlation between the first and second rating for
331 each subject. The correlations between the test and retest
332 values of the CBQ total score and the CBQ Core Index
333 subscale were 0.82 and 0.86 respectively. Both are
334 considered in excellent agreement (Fleiss, 1981).
335 Reliability of the CBQ screening algorithms was
336 assessed by comparing the diagnosis indicated by the
337 first rating for each subject to that indicated by the
338 second rating using a kappa coefficient. In this
339 comparison three classifications were used: BD
340 (DSM-IV phenotype), ADHD-only, and neither psychi-
341 atric diagnosis (see Table 2 for screening algorithms).
342 Based on the first rating, 85 (79%) were classified as
343 BD, 19 subjects (18%) were classified as ADHD, and 4
344 subjects (4%) were classified as having neither diagno-
345 sis. Within diagnostic group, the test–retest concordance
346 estimates were 0.81 for BD, 0.74 for ADHD, and 0.76
347 for neither diagnosis, all considered in excellent
348 agreement.

349 3.1.3. Inter-rater (inter-parent) reliability

350 Each of 48 subjects was rated once by each of two
351 different raters using the CBQ. In all cases, the first
352 responder was the mother of the child while the second
353 responder was most often the father (79%). Reliability
354 of the CBQ total score and the CBQ Core Index score
355 was assessed using a Pearson's correlation between the
356 first and second rating for each subject. The correlations
357 between the first and second values of the CBQ total
358 score and the Core Index score were 0.54 and 0.52
359 respectively, considered fair to good agreement (Fleiss,
360 1981). Reliability of the CBQ screening algorithms was
361 assessed by comparing the diagnosis indicated by the
362 first rating to that indicated by the second rating using a
363 kappa coefficient. The correlations within diagnostic
364 group were similar to that for the full set of subjects: for
365 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).

320 3.2. Construct validity

321 3.2.1. CBQ screening algorithms

322 Using the KSADS P/L, 76 subjects (56%) were
323 diagnosed with BD (DSM-IV phenotype), 21 subjects
324 (16%) with ADHD without mood disorder, and 38
325 subjects (28%) with no psychiatric diagnosis. Of the 76
326 subjects diagnosed with BD, 26 were diagnosed with
327 Bipolar I Disorder, 5 with Bipolar II Disorder, and 45
328 with Bipolar Disorder, Not Otherwise Specified (BP-
329 NOS). Those diagnosed with BP-NOS had manic
330 symptoms of briefer duration than required by DSM-
331 IV; the majority of these had rapid alternation of mood
332 states within the same day. The CBQ screening
333 algorithm for BD (DSM-IV phenotype) correctly
334 classified 57 of 59 subjects who did not have BD
335 (specificity=97%) and 58 of 76 subjects who had BD
336 (sensitivity=76%), yielding an overall kappa of 0.71.
337 Using the CBQ screening algorithms to differentiate
338 between three diagnostic groups, there was an overall
339 kappa of 0.69 (fair to good agreement) with an overall
340 rate of agreement of 81%. The CBQ screening algorithm
341 correctly classified all but 1 of the subjects with no
342 psychiatric diagnosis (97% correct screening). Fourteen
343 of the 21 ADHD subjects (67%) were correctly
344 classified, and 58 of the 76 BD subjects were correctly
345 classified (76%).

346 3.2.2. Validity of the CBQ Core Index

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

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

417 3.2.3. Using the CBQ to classify subjects into 418 subgroups with and without comorbid ADHD

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

438 3.2.4. Concurrent validity

439 Additional history data were obtained from the
440 parents of a subsample of 497 subjects, 325 of whom
441 had a community diagnosis of bipolar disorder. These
442 supplemental data included information such as age of
443 onset of psychiatric difficulties; current and first
444 psychiatric diagnoses; whether or not there was a
445 history of psychiatric hospitalization and, if so, how
446 many inpatient stays; duration of periods of mood
447 stability/instability, school difficulties (whether held
448 back in school); and presence/absence of involvement
449 with the juvenile justice system. We examined whether
450 CBQ total score differed between subgroups created
451 with these variables (Table 4). CBQ total score was
452 much higher among subjects with a parent-reported
453 primary diagnosis of bipolar disorder compared to all
454 other diagnoses. This contrast was statistically signifi-
455 cant. Similarly, children/adolescents reported to have
456 had prior psychiatric hospitalizations had much higher
457 scores, on average, on the CBQ than subjects who were
458 reported not to have been hospitalized. Children with an
459 early onset of psychiatric illness, dichotomized as onset
460 $\leq$ age 3 years vs. onset $>$ 3 years, had significantly
461 higher scores on the CBQ. On two important indicators
462 of functioning, school difficulties and involvement with
463 the juvenile justice system, parents reported a high
464 incidence of impairment, with fully 15% of parents

Table 4

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

History/event	n	CBQ Total	t4.3
Primary diagnosis	497		t4.4
Bipolar disorder	325	46.1 (8.6)	t4.5
Other	172	42.7 (10.1)	t4.6
z-statistic ^a		3.67, $p < 0.001$	t4.7
Hospitalizations, psych.	497		t4.8
One or more	189	48.3 (8.9)	t4.9
None	308	42.8 (8.9)	t4.10
z-statistic ^a		6.53, $p < 0.001$	t4.11
Symptom onset	497		t4.12
Onset $\leq$ 3 years	372	45.6 (9.2)	t4.13
Onset $>$ 3 years	125	42.8 (9.3)	t4.14
z-statistic ^a		3.15, $p = 0.002$	t4.15
School held-back	455		t4.16
At least one grade	71	48.6 (9.1)	t4.17
Never	384	44.6 (9.1)	t4.18
z-statistic ^a		3.34, $p = 0.001$	t4.19
Juvenile justice contact	497		t4.20
One or more times	57	48.4 (8.0)	t4.21
Never	440	44.5 (9.4)	t4.22
z-statistic ^a		3.03, $p = 0.003$	t4.23

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

t4.24

465 acknowledging school problems and 11% reporting
466 juvenile justice system problems. Among subjects
467 reported by parents to have been held back at school
468 at least 1 year, CBQ total scores were much higher than
469 comparable CBQ scores for all other subjects in the
470 subsample. Similarly, subjects reported by parents to
471 have had at least one incident resulting in involvement
472 with the juvenile justice system had much higher CBQ
473 scores than other subjects.

474 4. Discussion

475 Some of the most difficult questions surrounding
476 childhood-onset bipolar disorder have to do with
477 phenomenological issues. There is, as yet, no consensus
478 in the field on diagnostic criteria for the disorder as it
479 presents in children, although alternate disease pheno-
480 types have been proposed by several clinical investiga-
481 tors (Leibenluft et al., 2003; Geller et al., 2004; Papolos
482 et al., in press). The boundaries between the BD
483 syndrome and other psychiatric conditions of childhood
484 remain in debate, although clinicians consider this
485 crucial to appropriate therapeutic intervention (Sasson et
486 al., 2003; Kowatch et al., 2005). The psychiatric rating
487 scales heretofore available for rapid and cost-efficient
488 administration in research and clinical settings continue
489 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., 2005, *in press*).

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., in press). 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.

6. Uncited references

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