



Preliminary communication

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

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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.

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

1. Introduction

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

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

117 Brief screening instruments for childhood-onset BD
118 include the Parent General Behavior Inventory (P-GBI)
119 (Kahana et al., 2003), the Parent Young Mania Rating
120 Scale (P-YMRS) (Gracious et al., 2002), and the Child
121 Bipolar Questionnaire (CBQ). The P-GBI is adapted
122 from the GBI to assess children's mood disorder
123 symptoms. Parent responses identify mood states of
124 even modest severity with specificity and sensitivity in
125 children and adolescents (Findling et al., 2002; Young-
126 strom et al., 2001). A 10-item short form of the P-GBI
127 has been developed using Receiver Operating Charac-
128 teristic (ROC) analyses to identify the items with
129 maximum discriminating power (Youngstrom, 2004).
130 The P-YMRS is an 11-item Likert-scale instrument
131 derived from the YMRS as a parent-report version. Both
132 of these scales have performed well in psychometric
133 studies, and, as Youngstrom et al. (2004) point out in
134 their review of six potential screening instruments for
135 bipolar disorder in children, "the P-YMRS and P-GBI
136 produce fewer false alarms than the Achenbach scales
137 do because high scores are more specific to youths with
138 a bipolar diagnosis." The P-YMRS and the P-GBI focus
139 entirely on manic and hypomanic content—e.g., elated
140 mood, increased energy and activity, decreased sleep,
141 racing thoughts and pressured speech, hypersexuality—
142 and were not intended to diagnose alternate disease
143 phenotypes, identify subtypes, or investigate dimen-
144 sions of impairment associated with PBD.

145 The Child Bipolar Questionnaire (CBQ) was devel-
146 oped as a self-administered, parent-report measure to
147 establish initial eligibility for studies of childhood-onset
148 bipolar disorder sponsored by the Juvenile Bipolar
149 Research Foundation (JBRF). It was constructed based
150 on the model proposed by Depue et al. (1981), who,
151 with the development and validation of the General
152 Behavior Inventory (GBI), derived a dimensional
153 approach for the definition of bipolar disorder in adults.
154 For the CBQ, 85 items were drawn from DSM-IV
155 symptom criteria for mania, major depression, and
156 common comorbid conditions: separation anxiety
157 disorder, generalized anxiety disorder, obsessive–com-
158 pulsive disorder, oppositional defiant disorder, conduct

159 disorder, and attention-deficit disorder. Parents of a 159
160 clinical sample of children diagnosed with bipolar 160
161 disorder ($n=350$) were asked to rate the items on a 161
162 Likert scale: "1" ("never"), "2" ("sometimes"), "3"
163 ("often"), or "4" ("very often or almost constantly"). 163
164 Those items rated "2" or higher by >70% of the parents 164
165 were rank-ordered according to frequency of occur- 165
166 rence. Of these, the 65 highest ranked symptoms and 166
167 behaviors were included in the final version of the CBQ. 167

168 Several screening algorithms have been derived 168
169 from CBQ items in order to identify (1) possible BD 169
170 cases as defined by DSM-IV and the Narrow, Broad, 170
171 and Core phenotype symptom criteria, (2) possible BD 171
172 cases with and without comorbid ADHD and (3) 172
173 possible ADHD cases with no mood disorder. The 173
174 CBQ total score, a count of all items rated "3" ("often") 174
175 or "4" ("very often or almost constantly"), assesses 175
176 severity of illness. The Core Index subscale, scored in 176
177 the same manner, consists of 22 CBQ items determined 177
178 through factor analytic methods in a separate study to 178
179 represent prominent symptom dimensions of child- 179
180 hood-onset BD, including, but not limited to, manic 180
181 symptoms (Papolos et al., in press). Clinical features 181
182 relevant to the treatment of bipolar disorder such as 182
183 suicidality, aggressive behavior, and psychosis are also 183
184 assessed. 184

185 The CBQ has an estimated reading level of grade 185
186 8 and has been translated into Spanish, French, Polish, 186
187 and Portuguese. It may be self-administered by a 187
188 primary caretaker or completed by a clinician. Alone 188
189 or in combination with other instruments, the CBQ may 189
190 prove to be an effective screening tool for childhood- 190
191 onset BD for both clinical and research purposes. In this 191
192 report, we provide preliminary findings on the reliability 192
193 and validity of the CBQ in a sample of children recruited 193
194 via the JBRF data acquisition system. 194

195 2. Methods

196 2.1. Construction of CBQ diagnostic algorithms

197 In a prior study investigating the number of subjects 197
198 in the larger JBRF database potentially meeting 198
199 symptom criteria for each of the proposed alternate 199
200 phenotypes for childhood-onset BD, screening algo- 200
201 rithms were derived from CBQ items for the Narrow and 201
202 Broad phenotypes (Leibenluft et al., 2003) and a Core 202
203 phenotype proposed by the principal author (Papolos, in 203
204 press) (see Table 2). To attain a degree of confidence 204
205 about persistence of symptoms, the algorithms require 205
206 that a symptom be rated "4—very often or almost 206
207 constantly" to be counted as present. 207

t2.1	Table 2
t2.2	CBQ-derived screening algorithms
t2.3	<i>Narrow phenotype = rated 4 on:</i> "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	<i>Broad Phenotype = rated 4 on:</i> "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	<i>Core phenotype = DSM-IV Bipolar Disorder criteria are met (see below) and one of the following must be rated 4:</i> (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)	t2.9
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".	t2.10
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".	t2.9 t2.10
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".	t2.11 t2.12
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".	t2.13 t2.14
Occurrence of one or more items presented in parentheses is counted as one.	t2.15

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 241
242

243 carried out on CBQ data from a large subsample of the
 244 JBRF data set ($n=2795$) to test a hypothesis concerning
 245 the core symptom dimensions of childhood-onset BD
 246 (Papolos, in press). The CBQ items loading on the
 247 resulting factors comprise the Core Index subscale (see
 248 Table 3).

249 2.3. Sample

250 Since June 2000, parents or primary caretakers have
 251 participated in an online research program on a secure
 252 domain of the JBRF website, providing data on 5120
 253 children and adolescents, aged 5–17. Of these, 3430
 254 (66.9%) have been assigned the diagnosis of bipolar
 255 disorder by a clinician (child psychiatrist, psychiatrist,
 256 psychologist, pediatrician, or neurologist). The partici-
 257 pants in the research program are a self-selected
 258 sample, referred to JBRF through national advocacy
 259 sites, online newsletters, and professionals who treat
 260 children with bipolar disorder. Informed consent must
 261 be given before parents may enter data using JBRF's
 262 interactive data acquisition program. Data are stored
 263 using unique confidential parent and child ID numbers.
 264 The JBRF uses the Child Bipolar Questionnaire to
 265 determine potential eligibility for research studies and
 266 maintains email contact with the parents who submit
 267 this data to inform them of their children's initial
 268 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 269

Reliability assessment included three different meth- 270
 ods: internal consistency assessment, test–retest agree- 271
 ment, and inter-rater (virtually always, inter-parent) 272
 concordance. The internal consistency estimation was 273
 performed on a large CBQ data set ($n=2427$) using 274
 Cronbach's alpha procedure. The test–retest procedure 275
 was conducted by requesting via email that the first 100 276
 consecutive parents submitting CBQ data over the 277
 course of 3 months repeat their ratings within 7 days of 278
 their initial ratings. In this manner, test–retest data was 279
 collected on 108 children. The inter-rater reliability 280
 assessment was conducted similarly, with 50 consecu- 281
 tive parents requested to ask another parent or close 282
 family member to separately rate their child/adolescent 283
 within 7 days of each other. Inter-rater reliability data 284
 was collected on 48 children in this manner. Reliability 285
 of the CBQ total score, the CBQ Core Index subscale, 286
 and the CBQ-based screening algorithms was assessed. 287

2.5. Validity assessment procedures 288

A subsample of children from the larger data set were 289
 recruited for participation in JBRF-sponsored studies of 290
 childhood-onset BD, including a neuropsychological 291
 testing study of BD and ADHD-only group differences 292
 and a genetic study. Children without psychiatric 293
 disturbance were also recruited for comparison pur- 294
 poses. Eligibility for these studies required diagnostic 295
 confirmation via administration of the K-SADS P/L 296
 diagnostic interview to both parent and child. Parents 297
 and 135 children were interviewed by four graduate- 298
 level interviewers trained in the administration of the K- 299
 SADS P/L by the JBRF project director, who had been 300
 approved after training with Dr. Joan Kaufman. Three 301
 diagnostic groups were represented in the sample: BD 302
 (inclusive of BP I, BP II, and BP-NOS), ADHD-only, 303
 and no psychiatric diagnosis. Construct validity was 304
 assessed by comparing CBQ-based screening diagnosis 305
 with K-SADS P/L-based diagnosis. In addition, the 306
 CBQ Core Index subscale was assessed for its ability to 307
 predict membership in the three diagnostic groups. 308

Parents of a separate subsample of 497 children from 309
 the larger data set, 325 of whom had a community 310
 diagnosis of bipolar disorder, provided additional 311
 experiential and behavioral histories, such as prior 312
 psychiatric hospitalizations, school difficulties, and 313
 involvement with the juvenile justice system. Concur- 314
 rent validity was examined in this sample to determine 315
 whether CBQ total score differed among subgroups with 316
 differential experiences. 317

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. 366
These findings are comparable to the typical levels of 367
inter-rater agreement between adults describing a child's 368
behavior in the same setting (Achenbach et al., 1987). 369

370 3.2. Construct validity

371 3.2.1. CBQ screening algorithms

372 Using the KSADS P/L, 76 subjects (56%) were 372
diagnosed with BD (DSM-IV phenotype), 21 subjects 373
(16%) with ADHD without mood disorder, and 38 374
subjects (28%) with no psychiatric diagnosis. Of the 76 375
subjects diagnosed with BD, 26 were diagnosed with 376
Bipolar I Disorder, 5 with Bipolar II Disorder, and 45 377
with Bipolar Disorder, Not Otherwise Specified (BP- 378
NOS). Those diagnosed with BP-NOS had manic 379
symptoms of briefer duration than required by DSM- 380
IV; the majority of these had rapid alternation of mood 381
states within the same day. The CBQ screening 382
algorithm for BD (DSM-IV phenotype) correctly 383
classified 57 of 59 subjects who did not have BD 384
(specificity=97%) and 58 of 76 subjects who had BD 385
(sensitivity=76%), yielding an overall kappa of 0.71. 386
Using the CBQ screening algorithms to differentiate 387
between three diagnostic groups, there was an overall 388
kappa of 0.69 (fair to good agreement) with an overall 389
rate of agreement of 81%. The CBQ screening algorithm 390
correctly classified all but 1 of the subjects with no 391
psychiatric diagnosis (97% correct screening). Fourteen 392
of the 21 ADHD subjects (67%) were correctly 393
classified, and 58 of the 76 BD subjects were correctly 394
classified (76%). 395

396 3.2.2. Validity of the CBQ Core Index

397 To identify the differentiating power of the CBQ 397
Core Index, a discriminant analysis was performed 398
using the CBQ Core Index score as the only predictor 399
variable. The dependent variable used in this analysis 400
was the K-SADS diagnosis using the three groups: 401
PBD, ADHD, and no psychiatric diagnosis. From this 402
analysis it was determined that if the CBQ Core Index 403
subscale score was 0 or 1, a subject should be classified 404
as having no diagnosis; 36 out of the 38 subjects (95%) 405
were correctly classified. A subject with a CBQ Core 406
Index score of 2 or 3 was predicted to have ADHD-only. 407
Subjects with a score of 4 or higher were classified as 408
BD. The kappa coefficient for agreement between the 409
CBQ Core Index score with stated cut-offs and the K- 410
SADS diagnosis was 0.84, indicating excellent agree- 411
ment. After combining the normal and ADHD groups so 412
that the analysis consisted of BD vs. no BD, the CBQ 413
Core Index score with a cut-off of 4 had 100% 414

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	<i>n</i>	CBQ Total	
Primary diagnosis	497		t4.1
Bipolar disorder	325	46.1 (8.6)	t4.2
Other	172	42.7 (10.1)	t4.3
<i>z</i> -statistic ^a		3.67, $p < 0.001$	t4.4
Hospitalizations, psych.	497		t4.5
One or more	189	48.3 (8.9)	t4.6
None	308	42.8 (8.9)	t4.7
<i>z</i> -statistic ^a		6.53, $p < 0.001$	t4.8
Symptom onset	497		t4.9
Onset \leq 3 years	372	45.6 (9.2)	t4.10
Onset $>$ 3 years	125	42.8 (9.3)	t4.11
<i>z</i> -statistic ^a		3.15, $p = 0.002$	t4.12
School held-back	455		t4.13
At least one grade	71	48.6 (9.1)	t4.14
Never	384	44.6 (9.1)	t4.15
<i>z</i> -statistic ^a		3.34, $p = 0.001$	t4.16
Juvenile justice contact	497		t4.17
One or more times	57	48.4 (8.0)	t4.18
Never	440	44.5 (9.4)	t4.19
<i>z</i> -statistic ^a		3.03, $p = 0.003$	t4.20

^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

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

492 This report has presented preliminary psychometric
493 data on the Child Bipolar Questionnaire, a 65 item
494 parent-report rating scale that takes approximately
495 10 min to complete and lends itself easily to self-
496 administration via the internet or to administration by a
497 clinician. This screening instrument was originally
498 designed as a research tool to rapidly identify potential
499 BD cases for diagnostic confirmation and to assist in
500 defining subgroups for genotyping. The CBQ-based
501 scoring algorithms screen for those who may meet
502 symptom criteria for DSM-IV mania and several
503 alternate disease phenotypes. The Core Index subscale
504 of the CBQ represents key symptom dimensions in
505 childhood-onset BD that may be used to build
506 homogeneous subgroups for study. Finally, CBQ item
507 level data has been used to study factors associated with
508 suicide threat and with poor regulation of aggressive
509 behavior (Papolos et al., 2005, in press).

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

537 Overall kappa estimates may have been adversely
538 affected by two factors. First is the lack of fit of the
539 DSM-IV mania-based screening algorithm with the
540 clinical presentation of most of the children in the
541 sample. Of the 76 children given a K-SADS P/L

542 diagnoses of bipolar disorder, only 26 were diagnosed
543 with BP I. The majority of the children, 45 subjects,
544 were diagnosed with BP-NOS, a diagnosis that was
545 recommended for these children by experts at the NIMH
546 2001 Roundtable on Prepubertal Bipolar Disorder in the
547 absence of a more appropriate phenotype (NIMH,
548 2001). The CBQ Core Index subscale, a measure
549 based on analysis of symptom dimensions, performed
550 better than the BD and ADHD screening algorithms
551 when compared to K-SADS diagnoses, with a kappa
552 coefficient indicating excellent agreement. Another
553 factor that may have affected kappa estimates was the
554 attempt to classify children having ADHD (without
555 comorbid mood disorder) using the CBQ-based algo-
556 rithms. This attempt was not as successful as the effort to
557 differentiate children with bipolar disorder from those
558 without (inclusive of ADHD-only cases and those with
559 no psychiatric disorder). The CBQ was not designed to
560 diagnose ADHD per se, but to assist in the task of
561 differentiating the two diagnoses.

562 4.1. Limitations and caveats

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

592 al., 2001; Kim and Miklowitz, 2002), and inclusion of
 593 these cases can substantially reduce the diagnostic
 594 specificity of a test (as more non-BD cases score in the
 595 false positive range) (Youngstrom et al., in press). Also,
 596 few cases in the sample were diagnosed with Bipolar II
 597 disorder or cyclothymia. These are bipolar spectrum
 598 diagnoses that can be more difficult to recognize
 599 clinically or with screening measures (Miller et al.,
 600 2004; Youngstrom et al., 2001). We are currently
 601 conducting further assessments of CBQ validity in a
 602 large, diverse clinic population and in an inpatient unit
 603 of a children's psychiatric hospital.

604 5. Conclusion

605 With, as yet, no agreed upon uniform diagnostic
 606 criteria for bipolar disorder in children, it is a great
 607 challenge to develop a brief diagnostic instrument for
 608 youth that meets the needs of both researchers and
 609 clinicians. The Child Bipolar Questionnaire shows
 610 promise as a rapid and economically feasible way to
 611 screen for potential candidates meeting criteria for
 612 DSM-IV mania and several proposed alternate pheno-
 613 types. If further validation efforts are successful, the
 614 CBQ may be used by the clinician to aid in the early
 615 detection of BD features, the parsing of symptom
 616 dimensions and the differentiation of comorbid condi-
 617 tions for treatment focus. It may be used by researchers
 618 to aid in the further definition of the disease phenotype
 619 and the formation of more homogeneous pediatric
 620 samples for study of the neurobiology of bipolar
 621 disorder. The CBQ is available online at [http://jbrf.org/
 622 cbq/index.html](http://jbrf.org/cbq/index.html). An online scoring program for the CBQ
 623 is in development that provides total score and Core
 624 Index subscale score with diagnostic implications and a
 625 breakdown of symptom dimensions.

626 6. Uncited references

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