Juvenile Bipolar Research Foundation

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The Child Bipolar Questionnaire and four proposed phenotypes for juvenile-onset bipolar disorder

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Background

In 2001, the NIMH Roundtable on Prepubertal Bipolar Disorder (PBD) convened a panel of experts to review the growing literature on the prevalence and clinical presentation of PBD and to develop recommendations for future research (Special Communication, 2001). Members of the Roundtable suggested behavioral phenotypes for two groups of children: 1) those meeting the adult DSM-IV criteria for mania/hypomania and 2) those presenting differently from adults, but still severely impaired by symptoms of mood instability. The DSM-IV diagnosis Bipolar Disorder, Not Otherwise Specified (BP-NOS) was recommended as a "working diagnosis" to categorize the latter group of children for further study. Responding to a need for inclusion and exclusion criteria that might yield more homogeneous groups for research, investigators at the NIMH intramural program (Liebenluft et al., 2003) proposed four alternative phenotypes for pediatric bipolar disorder: the Narrow, Broad and two Intermediate Phenotypes.

In an effort to clearly discriminate PBD from ADHD and other childhood disorders characterized by irritability, the proposed Narrow Phenotype includes those children with the "hallmark symptoms" of elevated mood or grandiosity but excludes those diagnosed based on irritable mood alone. The Broad Phenotype includes children who have explosive rages, aggression, hyperarousal (hyperactivity, distractibility) and chronic mood disturbance, and excludes those who have elated mood or grandiosity. The two Intermediate Phenotypes include children with episodes of shorter duration and those with "irritable (hypo)mania." The NIMH panel recommended that future studies use DSM-IV diagnoses as "descriptive data" and substitute the proposed phenotype definitions as inclusion/exclusion criteria.

Extension of these phenotypic alternatives to include prominent dimensions of pediatric bipolar disorder in addition to mood state may be useful. Accordingly, we propose another phenotypic alternative, labeled the Core Phenotype, which combines categorical definitions of mania and specific functional impairments co-occurring with abrupt changes in mood. We examined the prevalence of, and interrelationships among, the Narrow, Broad, and Core phenotypes in a large database capturing parental reports of behaviors/symptoms related to juvenile-onset bipolar disorder.

Methods

Via a secure, internet-based data acquisition system established and maintained by the Juvenile Bipolar Research Foundation (JBRF), data were collected on 2,795 subjects screened for bipolar disorder using the Child Bipolar Parent Questionnaire (Papolos & Papolos 2002). The CBQ assesses behavior patterns typical of children and adolescents, ages 5-17, experiencing incipient, or fully-progressed, juvenile-onset bipolar disorder. The questionnaire was developed in response to the need for a screening instrument based on a dimensional model of bipolar disorder in children and adolescents. Items are keyed to the 65 symptoms and behaviors most commonly endorsed by parents of a large clinical sample of bipolar children and are answered on a Likert scale for frequency of occurrence.

Based on the symptoms reported on the CBQ, we constructed algorithms to identify subjects satisfying symptom criteria for three of the phenotypic alternatives: Narrow, Broad, and Core. Duration data were not available from the CBQ. To attain a degree of confidence about persistence of symptoms, we required that a symptom be rated "4 - Very often or almost constantly" to be counted as present.

We applied the algorithms to the CBQ database (N=2795) and counted index subjects nominally satisfying each of the four phenotypes. We examined the inter-phenotypic pairwise correlations among these four alternatives. In a subsample with KSADS diagnosis of bipolar disorder (largely bipolar-I and bipolar-NOS, with only a few bipolar-II subjects), we compared the frequencies with which the four phenotypes identified subjects with KSADS-assignments of each of the DSM-IV diagnoses.

Results

The algorithms identified large numbers of subjects satisfying the Narrow and Core phenotypes (~50 - 60%) and relatively small numbers of subjects satisfying the Broad phenotype (8.3%). Counts of index subjects satisfying the three algorithms are provided in Table 1. We found that a large proportion (≈92%) of the subjects satisfying Narrow phenotype criteria also satisfied Core phenotype criteria. 81% of those satisfying Broad phenotype criteria also satisfied Core phenotype criteria.

The CBQ items that appear most strongly to separate Narrow vs. Broad phenotypes, Core vs. Broad phenotypes, and Narrow vs. Core phenotypes are indicated in Table 2.

In the analyses based on KSADS data, both Narrow and Core phenotypes identified with high sensitivity, but low specificity, the subjects with KSADS bipolar-NOS diagnoses. These data are summarized in Table 3.

Conclusions

In reviewing the count of subjects satisfying criteria for the proposed phenotypes, we were not surprised by the number of subjects satisfying both Narrow and Core criteria. The central difference between these two phenotypes is the requirement of specific dimensions of impairment in the Core criteria set, e.g., aggressive behavior, attention deficits, and anxiety symptoms, that are not required in the Narrow criteria set. In our view, these features, which might be considered symptoms of comorbid disorders in subjects diagnosed with the Narrow criteria set, are pathognomonic of juvenile-onset bipolar disorder.

The relatively small number of subjects satisfying Broad criteria may be explained by the prevalence of elation and/or grandiosity, an exclusion criterion for the Broad phenotype.

An intriguing finding in the CBQ items differentiating phenotypes (Table 2) is the parent report of auditory/visual hallucinations and excessive risk-taking for approximately twice as many index subjects satisfying the Narrow and Core criteria as there were satisfying the Broad criteria. In a previous investigation, we found that auditory/visual hallucinations and excessive risk-taking were importantly related to parent reported suicidal threats by children/adolescents with community diagnosed bipolar disorder, independently of the risk associated with dysphoria (Papolos et al, 2005).

In anticipation of DSM-V, we believe that it is highly informative to attempt to identify what diagnostic prevalences can be expected with different definitional criteria of pediatric bipolar disorder. Investigations of how these phenotypic criteria are correlated with subject characteristics and outcome variables, as well as course of illness, may help us move toward a consensus about the cardinal symptoms of this condition in childhood.

References

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Table 1.

Counts of subjects (N=2795) satisfying phenotypic criteria for proposed phenotypes

Phenotype	Count (percent of total sample)	Overlap with Core
Narrow	1420 (50.8%)	1306
Broad	231 (8.3%)	187
Core	1747 (62.5%)	

Table 2.

Phenotypic contrasts—CBQ items (scored "4-very often or almost constantly") that discriminate Narrow, Broad and Core phenotypes, taken pairwise

A. Narrow vs. Broad:		Narrow	Broad	Ratio[a]	z[b]	p
1. CBQ 33	Has elated, silly, giddy mood states	82.0%	00.0%	----	----	----
2. CBQ 29	Has exaggerated ideas about self/abilities	65.6%	00.0%	----	----	----
3. CBQ 62	Has had auditory/visual hallucinations	16.5%	6.5%	2.54	8.3	<0.001
4. CBQ 30	Tells tall tales	54.3%	22.9%	2.37	19.1	<0.001
5. CBQ 36	Takes excessive risks	35.6%	15.2%	2.34	14.7	<0.001
6. CBQ 35	Inappropriate sexual behaviors	19.2%	9.1%	2.11	10.5	<0.001
7. CBQ 28	Has excessive and rapid speech	65.6%	32.5%	2.02	23.4	<0.001
8. CBQ 26	Has many ideas at once	67.7%	36.8%	1.84	23.8	<0.001
9. CBQ 34	Displays precocious sexual curiosity	25.7%	15.2%	1.70	11.5	<0.001
10. CBQ 61	Fascination with gore/blood/violence	27.9%	16.4%	1.69	10.4	<0.001
11. CBQ 63	Hoards or avidly collects objects/food	34.1%	22.9%	1.49	12.4	<0.001
12. CBQ 52	Lies to avoid consequences of actions	55.1%	39.8%	1.38	14.2	<0.001

B. Core vs. Broad:		Core	Broad	Ratio[a]	z[b]	p
1. CBQ 33	Has elated, silly, giddy mood states	67.1%	00.0%	----	----	----
2. CBQ 29	Has exaggerated ideas about self/abilities	50.4%	00.0%	----	----	----
3. CBQ 62	Has had auditory/visual hallucinations	15.3%	6.5%	2.35	9.05	<0.001
4. CBQ 36	Takes excessive risks	31.0%	15.2%	2.04	13.4	<0.001
5. CBQ 30	Tells tall tales	46.1%	22.9%	2.01	16.5	<0.001
6. CBQ 35	Inappropriate sexual behaviors	16.7%	9.1%	1.84	9.15	<0.001
7. CBQ 28	Excessive and rapid speech	55.2%	32.5%	1.70	19.0	<0.001
8. CBQ 34	Displays precocious sexual curiosity	24.1%	15.2%	1.59	11.2	<0.001
9. CBQ 26	Has many ideas at once	58.2%	36.8%	1.58	18.3	<0.001
10. CBQ 61	Fascination with gore/blood/violence	26.0%	16.5%	1.58	10.2	<0.001
11. CBQ 38	Has periods of low energy/withdrawal	44.3%	29.9%	1.48	15.4	<0.001
12. CBQ 39	Has decreased initiative	41.8%	29.0%	1.44	14.5	<0.001

C. Narrow vs. Core:		Narrow	Core	Ratio[a]	z[b]	p
1. CBQ 29	Has exaggerated ideas about self/abilities	65.6%	50.4%	1.30	8.64	<0.001
2. CBQ 33	Has elated, silly, giddy mood states	82.0%	67.1%	1.22	14.8	<0.001
3. CBQ 28	Has excessive and rapid speech	65.6%	55.2%	1.19	6.83	<0.001
4. CBQ 30	Tells tall tales	54.3%	46.1%	1.18	4.11	<0.001
5. CBQ 26	Has many ideas at once	67.7%	58.2%	1.16	4.49	<0.001
6. CBQ 35	Inappropriate sexual behaviors	19.2%	16.7%	1.15	3.37	<0.001
7. CBQ 36	Takes excessive risks	35.6%	31.0%	1.15	4.73	<0.001
8. CBQ 25	High frenetic energy and motor activation	83.0%	74.0%	1.12	3.07	0.002
9. CBQ 38	Has periods of low energy/withdrawal	40.1%	44.3%	1.10	-6.06	<0.001
10. CBQ 24	Easily excitable	76.0%	68.9%	1.10	3.04	0.002
11. CBQ 39	Has decreased initiative	38.1%	41.8%	1.10	-5.33	<0.001
12. CBQ 4	Hyperactive and easily excited in the PM	72.4%	66.1%	1.10	3.63	<0.001

a. Ratio is inverted when z-statistic is negative.
b. z-statistic estimated by logistic regression modeling, with adjustment for age/sex.

Table 3.

Proportions of subjects with/without a KSADS diagnosis of juvenile-onset bipolar disorder in each of four proposed phenotypes

Phenotypic Criteria		BP-I	KSADS Diagnosis[a] BP-NOS	Bipolar[b]
Narrow	Yes	8/31 (25.8%)	17/31 (54.8%)	27/31 (87.1%)
	No	8/24 (33.3%)	12/24 (50.0)	21/24 (87.5%)
Broad	Yes	0/4 (0%)	4/4 (100%)	4/4 (100%)
	No	16/51 (31.4%)	25/51 (49.0%)	44/51 (86.3%)
Core	Yes	9/36 (25.0%)	22/36 (61.1%)	33/36 (91.7%)
	No	7/19 (36.8%)	7/19 (36.8%)	15/19 (78.9%)

a. Tabulated in each cell are N=counts and (%) of KSADS cases identified vs. not identified by the phenotypic algorithm. The "Yes" row estimates sensitivity and the "No" row, specificity.
b. Bipolar means BP-I or BP-II or BP-NOS. There were insufficient BP-II cases to form a BP-II column in the table.