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Research report

# Factors associated with parent-reported suicide threats by children and adolescents with community-diagnosed bipolar disorder

Demitri Papolos<sup>a,b,\*</sup>, John Hennen<sup>a,c</sup>, Melissa S. Cockerham<sup>a</sup>

<sup>a</sup>The Juvenile Bipolar Research Foundation, 550 Ridgewood Rd., Maplewood, NJ 07040, United States

<sup>b</sup>Albert Einstein College of Medicine, Department of Psychiatry, Forchheimer Building, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461, United States

<sup>c</sup>Department of Psychiatry, Harvard Medical School, Boston, MA, and McLean Hospital, Belmont, MA 02478-9106, United States

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## Abstract

**Background:** It has recently been suggested that indicators of suicidality in youth may differ for different diagnostic groups [Horesh, N., Orbach, I., Gothelf, D., Efrati, M., Apter, A., 2003. Comparison of the suicidal behavior of adolescent inpatients with borderline personality disorder and major depression, *J. Nerv. Ment. Dis.* 191, 582–588.]. Aggression, impulsivity and risk-taking behaviors may be strong indicators of suicidality in children and adolescents with symptoms of bipolar disorder.

**Methods:** Parents completed the Child Bipolar Questionnaire (CBQ) via a secure, Internet-based data acquisition system. In multivariate modeling analyses, with age and sex as covariates, CBQ items that were most closely correlated with parent-reported suicide threat were identified. The strength of this multifactor association was then examined among subjects reported to have a community diagnosis of bipolar disorder compared to those who did not.

**Results:** In order of strength of association, the CBQ items most closely correlated with parent-reported suicide threat were: hallucinations, cursing/foul language, low energy/withdrawal, imagery—gore/violence, destroys property, poor self-esteem, excessive risk-taking, and excessive anxiety/worry. Of these 8 CBQ items, 3 (low energy, poor self-esteem, and anxiety/worry) have a dysphoric orientation, but the items with the strongest associations are related to psychosis, aggression and impulsivity. The association of the 8 CBQ items with suicidal threats was found to be much stronger in subjects with a reported prior or current bipolar diagnosis, compared with all other subjects.

**Limitations:** Child report data is not available. Parent report data has not yet been validated by research diagnostic interview.

**Conclusions:** The presence of aggression and impulsivity are importantly related to suicidal threats independently of the risk associated with dysphoria in children and adolescents who have been assigned a diagnosis of bipolar disorder or exhibit some

\* Corresponding author. Juvenile Bipolar Research Foundation, 550 Ridgewood Road, Maplewood, NJ 07040, Belmont. Tel.: +1 973 275 0400; fax: +1 973 275 0420.

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

symptoms of the disorder. This may have implications for treatment with antidepressant medication when the diagnosis of bipolar disorder may be present.

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## 1. Introduction

Suicide is the third leading cause of death among adolescents in the United States, accounting for 13.5% of all deaths in this age group (Murphy, 2000). Among children aged 5 to 14, suicide is the sixth leading cause of death, and among adolescents aged 15 to 19, suicide is the second leading cause of death (Anderson and Smith, 2003). On October 15, 2004, the U.S. Food and Drug Administration (FDA) issued a Public Health Advisory announcing a multi-pronged strategy to warn the public about the increased risk of suicidal thoughts and behavior (“suicidality”) in children and adolescents being treated with antidepressant medications (U.S. FDA, 2004). The agency ordered antidepressant manufacturers to add a “black box” warning to the health professional labeling of all antidepressant medications to describe this risk and emphasize the need for close monitoring of patients started on these medications.

This FDA action may have the effect of focusing public attention on depressive/dysphoric symptoms, the empirical connections between dysphoria and suicidality, and the antidepressant agents prescribed to treat these problems. In a recent report (American Academy of Child and Adolescent Psychiatry, 2001 [AACAP]) specifying “Practice parameter for the assessment and treatment of children and adolescents with suicidal behavior”, the following were identified as the important risk factors for suicidal behavior in children and adolescents:

|   |  |
|---|--|
| Males at much higher risk than females                              |  |
| Among males:  | Previous suicide attempts<br>Age 16 or older<br>Associated mood disorder<br>Associated substance abuse |
| Among females:  | Associated mood disorders<br>Previous suicide attempts   |
| Immediate risk predicted by agitation and major depressive disorder |  |

This AACAP admonition, while using the terms “associated mood disorder” and/or “agitation”, does not specifically address the elements of aggressiveness, impulsivity, risk-taking, excessive anxiety, and fear-of-harm that are considered by some observers to be highly correlated with suicidality in many adolescents and preadolescents (Horesh et al., 1999; Goodwin and Hamilton, 2002; Rujescu et al., 2003; Miotto et al., 2000; Papolos et al., submitted for publication).

We believe that the current focus of discussion on the connections between antidepressants and suicidality in children and adolescents, while important, may suggest that depressive/dysphoric indicators apply equally to all diagnostic groups, underemphasizing the contribution of other indicators such as aggression, excessive anxiety, impulsivity and risk-taking behaviors. These indicators may be strongly associated with suicide in children and adolescents in particular diagnostic groups, such as those with bipolar disorder and the bipolar spectrum disorders, 25% to 50% of whom attempt suicide at least once according to one review of the literature (Tondo et al., 1999), with a lifetime risk of suicide attempts highest in those with bipolar II disorder, bipolar I disorder and major depressive disorder, respectively, according to another review (Rihmer and Pestalicy, 1999). Recent work on treatment-emergent mania suggests that treatment with mood-elevating agents in children diagnosed with bipolar disorder may induce new manic symptoms and psychotic or aggressive behavioral changes in up to half of cases exposed to an antidepressant (Faedda et al., 2004).

Accordingly, we assembled data provided by parents/guardians accessing the Juvenile Bipolar Research Foundation website, identifying the behavioral factors most closely correlated with a positive response to a direct question about suicidality in their children. Specifically, we examined parental responses to the direct query: “Has [your child] made direct threats of suicide” with frequency “Very

often or almost constantly”. We summarize these correlative data in this report.

## 2. Methods

### 2.1. Data acquisition

The Juvenile Bipolar Research Foundation (JBRF) has established an extensive, Internet-based system for contact with families with one or more children who have been clinically diagnosed with bipolar disorder or have evidenced behavioral patterns suggestive of juvenile-onset bipolar disorder or any of several closely related neuropsychiatric difficulties (JBRF, 2004). In a carefully controlled, secure, website-based system, parents and guardians of children and adolescents previously diagnosed with bipolar disorder or having exhibited symptoms of bipolar disorder of sufficient intensity and severity to cause the parents to seek professional evaluation may elect to provide information confidentially about the behaviors of the affected offspring. All of the children and adolescents were assessed using the Child Bipolar Questionnaire (CBQ), a 65-item behavioral assessment instrument appropriate for use in the assessment of behavior patterns typical of children and adolescents experiencing incipient, or even fully progressed, juvenile-onset bipolar disorder (Papolos et al., submitted for publication). These rating scale data, after being passed through validation screens, have been maintained within the JBRF system in instrument-specific databases, coded by unique, confidential family and child identification numbers, with linkage across rating scales achievable via these ID numbers.

### 2.2. CBQ item scoring

The CBQ items are scored on a 4-point scale (1 to 4, with higher numbers indicating greater severity). We used CBQ Item 60 (“Has made clear threats of suicide”), with frequency score 4 (“very often or almost constantly”) to identify subjects whom the parents considered to be at risk for suicidality. We labeled this indicator “suicide-threat”, thereby defining two subgroups, the “suicide-threat-present” group vs. all other subjects. We then summarized item-level

data for the remaining CBQ items by dichotomizing the responses, separating parental responses 1–2 (“never or hardly ever” and “sometimes”) from responses 3–4 (“often” and “very often or almost constantly”). We contrasted these dichotomized CBQ item-scores between subjects with/without the suicide-threat indicator. There was one exception to this procedure: we omitted this contrast for CBQ item 58 (“makes moderate threats to others or self”) and item 59 (“makes clear threats of violence to others or self”) because of the close, almost redundant connection between the content of these items and that of CBQ item 60 (“has made clear threats of suicide”).

### 2.3. Analyses employed

In a sequence of modeling analyses with parent-reported suicide threat (frequency 3 or 4 on CBQ item 50) as the dependent measure, we identified CBQ items that were strongly correlated with this binary outcome. In all of these analyses, we included sex and age covariates, with age dichotomized at 10 years (age=10 years vs. age >10 years). Suicidal-threat rates were reported as percentages with 95% confidence intervals (95% CI). We used generalized linear modeling (GLM) methods (binomial family with logarithmic link) to carry out this predictor-selection procedure (Hardin and Hilbe, 2001). In these binary outcome GLM analyses, adjusted risk ratios (RR) and their 95% confidence intervals (95% CI) were estimated. The selection criterion used to decide which CBQ items were to be included in the best item-predictor set (together with age/sex) was change in the log-likelihood function that is a bi-product of GLM regression modeling.

### 2.4. Stratification by dysphoric/depressive symptoms

Based on several CBQ items assessing dysphoria or depressive symptoms, we constructed a subscale score to serve as a proxy for level of parent-ascribed depression/dysphoria for each subject. Seven items were included in this proxy index: CBQ item 2 (exhibits excessive anxiety or worry), CBQ 7 (sleeps fitfully, or awakens in the night), CBQ 13 (inability to concentrate at school), CBQ 38 (has low energy and/or withdrawal/isolation), CBQ 39 (decreased initiative), CBQ 40 (periods of self-doubt and poor self-

esteem), and CBQ 41 (feels easily criticized and/or rejected). In forming this summary dysphoria indicator, we summed all 4 levels of the 7 CBQ items, rather than the dichotomized forms of the item responses. We then included this summary depressive indicator as a covariate in the GLM models assessing the risk ratios for suicide-threat associated with the 8 CBQ items most strongly predictive of suicidality. This yielded adjusted risk ratios and their 95% CIs. We repeated these modeling analyses, comparing subjects with relatively low-severity depressive symptoms (first quintile) with the remaining four-fifths of the study sample.

### 2.5. General statistical methods

Averaged continuous data are reported as means with standard deviations (mean  $\pm$  S.D.) or 95% CI. Binary data are reported as  $N$  (%) or  $N$ /denominator (% with 95% CI). Some continuous variables were logarithmically transformed to achieve more nearly Gaussian distributions. Robust standard error (SE) estimates were obtained whenever feasible. Goodness-of-fit of GLM models was checked with partial-residual plots. Statistical significance required 2-tailed  $p \leq 0.05$ . Analyses employed commercial microcomputer programs (Stata<sup>®</sup>, Stata Corporation, College Station, TX).

## 3. Results

There were 2479 subjects for whom CBQ data were obtained via the JBRF internet-based system.

For 379 (15.3%) of these subjects (95% CI 13.9–16.8%), it was reported by the parent that they make “clear threats of suicide” with frequency “very often or almost constantly”. Included in this suicide-threat subgroup were 139 girls (34.2%) and 240 boys; average age was  $10.8 \pm 3.8$  years (median 10.6).

### 3.1. Age and sex associations with suicide threat

There was no difference in the proportion of boys and girls whose parents reported that they had made suicide threats (15.4% vs. 11.3%, Table 1). Older subjects were much more likely than younger children to be identified as having threatened suicide (Table 1). This difference was strongly statistically significant ( $\chi^2 [df=1]=25.0, p<0.001$ ).

### 3.2. CBQ item-level associations with suicide threat

In multivariate regression analyses, we selected the several CBQ items that were most strongly associated with suicide-threat status. In advance of initiating the study, we had anticipated that in our sample, comprised of children either assigned a diagnosis of bipolar disorder or whose parents reported some symptoms of the disorder, CBQ items related to aggression and/or impulsivity would be strongly correlated to suicidal threat. Accordingly, we started our analyses with CBQ items assessing aggression-related issues and added other CBQ items that empirically increased the model log likelihood function. This process resulted in the selection of 8 factors that, in multivariate models

Table 1  
Characteristics of study subjects

| Measure                       | Suicidal threats          | All others                | $\chi^2$ or $z^a$ | $p$    |
|-------------------------------|---------------------------|---------------------------|-------------------|--------|
| Number                        | 379 (15.3%)               | 2100 (84.7%)              | –                 | –      |
| Males                         | 240 (15.4%)               | 1314 (84.6%)              | 0.08              | 0.78   |
| Age ( $N=2456$ )              | $12.0 \pm 3.6$ (mdn 11.8) | $10.6 \pm 3.8$ (mdn 10.4) | 6.61              | <0.001 |
| Medications                   |                           |                           |                   |        |
| Mood stabilizers ( $N=1291$ ) | 228 (17.7%)               | 1063 (82.3%)              | 11.7              | 0.001  |
| Antidepressants ( $N=652$ )   | 117 (17.9%)               | 535 (82.1%)               | 4.82              | 0.028  |
| Anti-ADHD ( $N=749$ )         | 114 (15.2%)               | 635 (84.8%)               | 0.01              | 0.95   |
| CBQ total score               | $50.6 \pm 8.8$            | $42.1 \pm 10.8$           | 16.8              | <0.001 |

<sup>a</sup> Reported are  $N$  (%) and mean  $\pm$  S.D. for categorical and continuous contrasts, respectively. Statistical significance assessed using  $\chi^2 [df=1]$  for categorical and  $z$  for continuous contrasts.

with adjustment for age and sex, were found to have the strongest associations with parent report of suicide threat. These were: CBQ 62 (has acknowledged experiencing hallucinations), CBQ 57 (curses viciously, uses foul language), CBQ 38 (has periods of low energy or withdrawal/isolation), CBQ 61 (fascination with gore/violent imagery), CBQ 56 (has destroyed property intentionally), CBQ 40 (experiences periods of self-doubt and poor self-esteem), CBQ 36 (excessive risk-taking), and CBQ 2 (exhibits excessive anxiety and worry). When combined in a multivariate model, together with age and sex, all of these factors were found to be significantly correlated with parent-reported suicide threat (Table 2). The strongest of these associations was for CBQ 62 (hallucinations), for which the adjusted risk ratio was 1.82 (95% CI 1.52–2.19, Table 2), indicating that, among children acknowledging hallucinations, the proportion of children making suicide threats “very often or almost constantly”, was 80% greater than among children absent or at least not acknowledging the occurrence of hallucinations.

Following the risk modeling summarized in Table 2, we constructed the corresponding receiver-operating-characteristic (ROC) curve and obtained the associated specificity and sensitivity estimates. With

the 10 factors summarized in Table 2 (8 CBQ items plus age and sex), the predictive accuracy of the multivariate model in identifying suicide-threat status was estimated to be 85.6%. Specificity (97.8%) was very high for this model, while sensitivity was quite weak (17.2%). The area under the ROC curve was 0.80 (Fig. 1).

Among the 8 CBQ factors summarized in Table 2 in terms of their associations with parent-reported suicide threat, 3 are clearly identified as measures of dysphoria/depressive. These items are CBQ 38 (has periods of low energy or withdrawal/isolation), CBQ 40 (experiences periods of self-doubt and poor self-esteem), and CBQ 2 (exhibits excessive anxiety and worry). The remaining 5 CBQ factors, and those with the strongest associations, are measures of psychosis (CBQ 62 [hallucinations]), aggression (CBQ 57 [cursing], CBQ 56 [destroys property]), (CBQ 61 [violent or gory imagery]), and impulsivity (CBQ 36 [risk-taking]).

### 3.3. CBQ item correlations with suicide-threat among subjects stratified by severity of dysphoric symptoms

We repeated the above analyses after adjusting for a summary measure of dysphoria/depression

Table 2  
CBQ items most closely correlated with suicidality index

| Measure                          | Factor               |                     | Risk ratio <sup>a</sup> | 95% CI     | z    | p      |
|----------------------------------|----------------------|---------------------|-------------------------|------------|------|--------|
|                                  | Present <sup>b</sup> | Absent <sup>b</sup> |                         |            |      |        |
| Number of subjects               | 379 (15.3%)          | 2100 (84.7%)        | –                       | –          | –    | –      |
| Age/sex                          |                      |                     |                         |            |      |        |
| Sex (males)                      | 240 (15.4%)          | 1314 (84.6%)        | 1.07                    | 0.91, 1.26 | 0.81 | 0.42   |
| Age (age >10 years)              | 246 (18.5%)          | 1082 (81.5%)        | 1.20                    | 0.99, 1.45 | 1.93 | 0.053  |
| CBQ items                        |                      |                     |                         |            |      |        |
| Item 62 (hallucinations)         | 174 (31.3%)          | 382 (68.7%)         | 1.82                    | 1.52, 2.19 | 6.43 | <0.001 |
| Item 57 (cursing, foul language) | 276 (23.9%)          | 877 (76.1%)         | 1.76                    | 1.40, 2.20 | 4.87 | <0.001 |
| Item 38 (low energy/withdrawal)  | 316 (20.6%)          | 1218 (79.4%)        | 1.80                    | 1.38, 2.35 | 4.34 | <0.001 |
| Item 61 (imagery—gore/violence)  | 237 (25.0%)          | 710 (75.0%)         | 1.53                    | 1.25, 1.88 | 4.09 | <0.001 |
| Item 56 (destroys property)      | 308 (21.0%)          | 1160 (79.0%)        | 1.65                    | 1.29, 2.12 | 3.98 | <0.001 |
| Item 40 (poor self-esteem)       | 356 (18.4%)          | 1576 (81.6%)        | 2.13                    | 1.40, 3.25 | 3.51 | <0.001 |
| Item 36 (excessive risk-taking)  | 255 (21.6%)          | 923 (78.3%)         | 1.37                    | 1.12, 1.68 | 3.08 | 0.002  |
| Item 2 (excessive anxiety)       | 308 (17.6%)          | 1439 (82.4%)        | 1.36                    | 1.08, 1.70 | 2.61 | 0.009  |

<sup>a</sup> Risk ratio and its 95% confidence interval estimated by generalized linear regression modeling (GLM) with presence/absence of prevalent suicidal threats (CBQ Item 60) as the outcome measure. The risk ratio estimates were all derived within a common multivariate model.

<sup>b</sup> Reported are N (%) of subjects responding positively (“Present”) to each CBQ item, except that, for age/sex, “Present” means male and age >10 years, respectively.

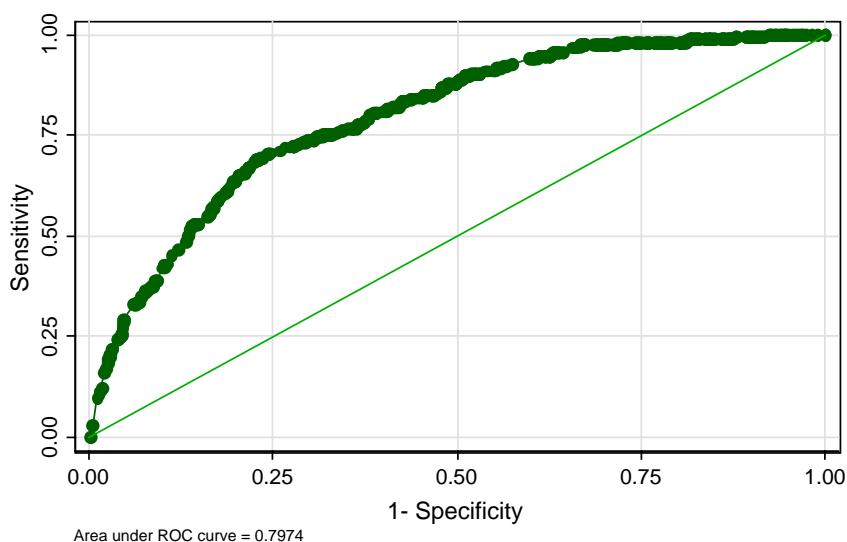


Fig. 1. ROC curve—suicide threat predicted by 8 CBQ items with age/sex adjustment.

extracted from the CBQ results. We summed the item level scores of the 7 items that, by content, appear to be conventional indicators of dysphoria/depression. These are: CBQ 2 (exhibits excessive anxiety and worry), CBQ 7 (sleeps fitfully and/or awakens in the night), CBQ 13 (inability to concentrate in school), CBQ 38 (has periods of low energy and/or withdrawal/isolation), CBQ 39 (decreased initiative), CBQ 40 (has periods of self-doubt and poor self-esteem), and CBQ 41 (feels easily criticized and/or rejected). We then repeated the modeling, including this summary depression/dysphoria score together with the 5 CBQ items not obviously dysphoria-related (i.e., CBQ items 62 [hallucinations], 57 [cursing, foul language], 61 [gore/violent images], 56 [destroys property], and 36 [excessive risk-taking]). Results are summarized in Table 3. Table 3 risk ratio estimates differ only marginally from their counterparts in Table 2.

We repeated this modeling procedure, limiting the analysis to subjects with the lowest summary depressive/dysphoria subscale scores (that is, the lowest 20% on this ad hoc measure of dysphoria/depression). Limiting the study sample in this manner resulted in a subset of size  $N=605$ . The results of this analysis were quite similar to the results summarized in Table 3, except that, because of the substantially reduced sample size, the

predictive power is attenuated. In this reduced sample analysis, the estimated risk ratios for the 5 CBQ items of interest were as follows:

The first four risk ratio estimates above are in the range circa 2.0 to 2.5, indicating at least a doubling of

Table 3  
CBQ items closely correlated with suicidality index, with adjustment for depressive/dysphoric symptom levels ( $N=2456$ )

| Measure                              | Risk ratio <sup>a</sup> | 95% CI <sup>a</sup> | <i>z</i> | <i>p</i> |
|--------------------------------------|-------------------------|---------------------|----------|----------|
| Sex (males)                          | 1.09                    | 0.93, 1.27          | 1.09     | 0.28     |
| Age (age >10 years)                  | 1.22                    | 1.03, 1.46          | 2.24     | 0.025    |
| CBQ items                            |                         |                     |          |          |
| Item 62 (hallucinations)             | 1.71                    | 1.41, 2.06          | 5.53     | <0.001   |
| Item 57 (cursing, foul language)     | 1.69                    | 1.34, 2.13          | 4.41     | <0.001   |
| Item 56 (destroys property)          | 1.62                    | 1.26, 2.07          | 3.80     | <0.001   |
| Item 61 (gore/violent imagery)       | 1.46                    | 1.18, 1.80          | 3.55     | <0.001   |
| Item 36 (excessive risk-taking)      | 1.22                    | 0.98, 1.51          | 1.84     | 0.066    |
| Proxy score for depression/dysphoria | 1.12                    | 1.10, 1.16          | 8.02     | <0.001   |

<sup>a</sup> Reported are adjusted risk ratios and their 95% confidence intervals estimated by generalized linear regression modeling (GLM) with presence/absence of prevalent suicidal threats (CBQ Item 60) as the outcome measure.

suicidality risk associated with each of these four CBQ items. These data suggest that, even when depressive/dysphoric symptoms are apparently not so

| CBQ item                         | Risk ratio | 95% CI     | z-statistic | p     |
|----------------------------------|------------|------------|-------------|-------|
| Item 62 (hallucinations)         | 1.98       | 0.80, 4.87 | 1.48        | 0.14  |
| Item 57 (cursing, foul language) | 2.53       | 1.07, 5.99 | 2.12        | 0.034 |
| Item 61 (imagery—gore/violence)  | 2.21       | 0.86, 5.71 | 1.64        | 0.10  |
| Item 56 (destroys property)      | 2.04       | 0.85, 4.91 | 1.60        | 0.11  |
| Item 36 (excessive risk-taking)  | 1.01       | 0.39, 2.58 | 0.01        | 0.99  |

prominent, the elements assessed by these several CBQ items are strongly correlated with parent-reported suicide-threat.

Obviously, the data of Table 3 do not argue that depression/dysphoria symptoms are unrelated to suicidality. The important implication of Table 3 results is that, even after adjusting for this dysphoria/depression effect, the remaining explanatory factors all have risk ratios substantially in excess of the null value of unity. Moreover, in the results for the reduced model (limited to the lowest quintile on the summary dysphoria/depression measure), 4 of the 5 risk ratio estimates (all but that for CBQ item 36) indicate a doubling or more of risk to be associated with these items, with risk ratio estimates that are even larger than their counterparts in the full model (Table 3).

One interpretation of these data is that the presence of psychotic symptoms, aggressive behavior and impulsivity is importantly related to suicidal threat independently of the risk associated with dysphoria.

### 3.4. Current or prior diagnosis of bipolar disorder

By parental report, data were available on whether or not a diagnosis of bipolar disorder (BPD) had been assigned either currently or in the past. Among subjects for whom this parent-reported diagnostic indicator was available, 1728/2479 (69.7%, 95% CI 67.9–71.5%) had been ascribed a bipolar disorder diagnosis. Parent-reported suicide threat was much more common in subjects reported to have had a

bipolar diagnosis (316/1728 [18.3%]) than among subjects who had not received this diagnosis (63/751 [8.4%]). The adjusted risk ratio (adjusted for sex/age) for this bipolar diagnosis indicator was 2.29 (95% CI 1.71 to 3.05,  $z=5.63$ ,  $p<0.001$ ).

We expected that the 8 CBQ items that we found to be the most strongly associated with suicide threat in the entire sample would be more strongly associated with suicide threat in the subsample of children who had been assigned a bipolar diagnosis compared to those who had not been assigned such a diagnosis. In a chi-square test (using seemingly unrelated regression modeling methods (Greene, 2000)), with degrees of freedom=10, reflecting use of the 8 CBQ items plus age and sex as explanatory factors in the regression modeling, we found that this expectation was supported in the data. The multivariate correlation of the 10 explanatory factors was much stronger in the subgroup with a parent-reported bipolar disorder diagnosis than in all other children:  $\chi^2 [df=10]=20.1$  ( $p=0.028$ ).

We then carried out modeling analyses examining the pairwise interactions between BPD diagnosis and the 8 CBQ items found to be strongly associated with suicide threats. In two of these modeling analyses, the interactions between BPD and the CBQ item were found to be statistically significant. For the remaining 6 CBQ items, the associations were in the same direction, but they were not statistically significant (data not shown). The two CBQ items for which there were significant associations were CBQ 62 (hallucinations) and CBQ 61 (fascination with gore/violent imagery). The combinations of BPD–hallucinations ( $z=2.62$ ,  $p=0.009$ ) and BPD–gore/violent imagery ( $z=2.66$ ,  $p=0.008$ ) were associated with higher rates of parentally identified severe and frequent suicidal threats. For the BPD–hallucinations combination, the percentage of subjects with suicidal threats was 32.4% vs. 11.3% for all other subjects. For the BPD–violent imagery combination, the percentage of subjects with suicidal threats was 27.8% vs. 10.3% for all other subjects. In summary, the association between the 8 CBQ items with suicidal threats was found to be much stronger in subjects with a reported prior or current bipolar diagnosis, compared with all other subjects.

### 3.5. Results summary

In summary, we found a high rate of parental report of very frequent and clear threats of suicide being made by their adolescent and preadolescent offspring, exceeding 15% (95% CI 13.9–16.7%) across the entire Internet-based study sample. Parent-reported suicide threat was much more common in subjects reported to have had a bipolar diagnosis (316/1728 [18.3%]) than among subjects who had not received this diagnosis (63/751 [8.4%]). There was no sex difference in this rate, but there was a strong positive correlation with age. In order of strength of association, the CBQ items most closely correlated with the parent-reported suicide threats were: hallucinations, cursing/foul language, low energy/withdrawal, imagery—gore/violence, destroys property, poor self-esteem, excessive risk-taking, and excessive anxiety/worry. The association between these factors and parent-reported suicide threats was much stronger in children/adolescents with community-diagnosed bipolar disorder than in subjects not being reported to have been ascribed this diagnosis.

## 4. Discussion

In undertaking this study, we expected to find that, in a sample of children with some indication of bipolar disorder, parents reporting aggressive behavior and impulsivity in their children would also report frequent serious suicide threats. The available data, summarized in this report, strongly support this expectation. Parental report of suicidal threat, frequent or otherwise, is not the same as actual suicide threat, and certainly not a direct proxy for suicidal acts or gestures. Yet, neither are there obvious factors operative in this situation that would cause one to doubt the validity of parent-reported suicidal threats.

The CBQ items identified by parents as commonly co-occurring with frequent and severe suicidal threats (Table 2: hallucinations, cursing/foul language, withdrawal, imagery of gore/violence, destroys property, low self-esteem, excessive risk-taking, excessive anxiety) may be considered measures of severity of illness, and thus understandably related to suicidality. However, a striking feature of the

behavioral profile conveyed by these data is that parent-reported suicidal threat appears to be much more weakly associated with parent-reported dysphoric indicators than with parent-reported impulsive/aggressive indicators. Among the 8 most prominent behavioral factors summarized in Table 2 as being most closely correlated with severe and frequent suicidal threats, 3 (withdrawal, low self-esteem, and anxiety) are typically associated with depression. The majority are indicative of aggression, impulsivity, and psychosis.

Any conclusions about the weight to be given to depressive/dysphoric indicators vs. aggressive/impulsive indicators are necessarily limited by the absence of child report information in these data. However, parent-report data suggest that aggression and impulsivity are importantly related to suicidal threats independently of the risk associated with dysphoria. Clinicians treating children and adolescents, if they are to be vigilant to the risk of suicide, need to be fully aware of the potential contributions of all of these indicators, especially in combination with each other.

If replicated, these findings may have important implications for the clinical assessment and management of suicidality in children and adolescents at risk for or already diagnosed with bipolar disorder. Children/adolescents who carry a diagnosis of bipolar disorder could be assessed for psychosis, aggressive behavior and impulsivity as especially indicative of potential suicidality and, if such indications were found to be present, antidepressant medication could either be avoided or, if used, very carefully monitored. Similarly, children/adolescents who become suicidal on antidepressant medication could be assessed for bipolar disorder, with particular attention to symptoms of psychosis, aggression, and impulsivity.

Limitations of the study are several: the data were assembled via parental report through an Internet-based data acquisition system. We have not yet validated the parental report data. Similarly, community diagnoses, obtained via the JBRF Internet-based data acquisition system, have not yet been validated through research diagnostic methods. This effort, using the Kiddie-Schedule for Affective Disorders and Schizophrenia—Present and Lifetime system (K-SADS P-L) with both parent and child, is currently underway.



In summary, we report very strong correlations between parental-report of psychosis, aggression and risk-taking propensities and parental-report of frequent and persistent threat-of-suicide that may have important diagnostic and treatment implications.

## References

- American Academy of Child and Adolescent Psychiatry, 2001. Practice parameter for the assessment and treatment of children and adolescents with suicidal behavior. *J. Am. Acad. Child Adolesc. Psych.* 40, 24S–51S.
- Anderson, R.N., Smith, B.L., 2003. Deaths: leading causes for 2001. *Natl. Vital Stat. Rep.* 52, 1–86.
- Faedda, G.L., Baldessarini, R.J., Glovinsky, I.P., Austin, N.B., 2004. Treatment-emergent mania in pediatric bipolar disorder: a retrospective case review. *J. Affect. Disord.* 82, 149–158.
- Goodwin, R.D., Hamilton, S.P., 2002. The early-onset fearful panic attack as a predictor of severe psychopathology. *Psychiatry Res.* 109, 717–719.
- Greene, W.H., 2000. *Econometric Analysis*, 4th ed. Prentice-Hall, Upper Saddle River, NJ.
- Hardin, J.W., Hilbe, J., 2001. *Generalized Linear Models and Extensions*. Stata Press, College Station, TX.
- Horesh, N., Gothelf, D., Ofek, H., Weizman, T., Apter, A., 1999. Impulsivity as a correlate of suicidal behavior in adolescent psychiatric inpatients. *Crisis: J. Crisis Interv. Suicide* 20, 8–14.
- Horesh, N., Orbach, I., Gothelf, D., Efrati, M., Apter, A., 2003. Comparison of the suicidal behavior of adolescent inpatients with borderline personality disorder and major depression. *J. Nerv. Ment. Dis.* 191, 582–588.
- JBRF (Juvenile Bipolar Research Foundation) 2004. [www.bpchildresearch.org](http://www.bpchildresearch.org).
- Miotto, P., De Coppi, M., Frezza, M., Petretto, D., Masala, C., Preti, A., 2000. Suicidal ideation and aggressiveness in school-aged youths. *Psychiatry Res.* 120, 247–255.
- Murphy, S.L., 2000. Deaths: final data for 1998. *Natl. Vital Stat. Rep.* 48, 101–105.
- Papolos, D., Hennen, J., Cockerham, M.S., submitted for publication. Fear-of-harm anxiety and overt aggressive behaviors directed at self and others in children/adolescents with probable juvenile-onset bipolar disorder. *J. Affect. Disord.*
- Rihmer, Z., Pestalicy, P., 1999. Bipolar II disorder and suicidal behavior. *Psychiatr. Clin. North Am.* 22, 667–673.
- Rujescu, D., Giegling, I., Sato, T., Hartmann, A.M., Moller, H.J., 2003. Genetic variations in tryptophan hydroxylase in suicidal behavior: analysis and meta-analysis. *Biol. Psychiatry* 54, 465–473.
- Tondo, L., Baldessarini, R.J., Hennen, J., 1999. Lithium and suicide risk in bipolar disorder. *Prim. Psychiatry* 6, 51–56.
- U.S. Food and Drug Administration, 2004. FDA Launches a Multi-Pronged Strategy to Strengthen Safeguards for Children Treated With Antidepressant Medications. FDA News-For Immediate Release, Washington, DC. Oct. 15.