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Research paper

Obsessive fears about harm to self or others and overt aggressive behaviors in youth diagnosed with juvenile-onset bipolar disorder

Demitri Papolos^{a,b,*}, John Hennen^{a,c,d}, Melissa Cockerham^a

^a Juvenile Bipolar Research Foundation, 550 Ridgewood Rd., Maplewood, NJ 07040, United States

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

^c Department of Psychiatry, Harvard Medical School, Boston, MA, United States

^d McLean Hospital, Belmont, MA 02478-9106, United States

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Abstract

Background: Obsessive fear-of-harm, either fear of doing harm or fear of harm coming to self, may be closely associated with aggressive behaviors in juvenile-onset bipolar disorder.

Methods: We analyzed parent-report data on the Yale–Brown Obsessive Compulsive Scale (YBOCS) and Overt Aggression Scale (OAS) for 1601 children/adolescents with a clinician-assigned diagnosis of bipolar disorder. The summing of 6 YBOCS items rated “often” or “very often or almost constant” yielded a biphasic distribution of scores. Median-split was used to define meaningful subgroups contrasting high vs. low “fear-of-harm”, which were then compared on parent-reported severe injury to self and others and on parent-reported suicide threats.

Results: High fear-of-harm was strongly associated with parent-reported severe injury to self and others. For self-injury, the estimated risk ratio for high vs. low fear-of-harm subgroups was 2.68 (95% confidence interval 1.87–3.86), indicating greater than doubling of risk associated with high fear-of-harm. For severe injury to others, the estimated risk ratio was 7.97 (95% confidence interval 4.19–15.2), suggesting a nearly eight-fold increased risk associated with high fear-of-harm. High fear-of-harm subjects were reported to make serious suicide threats much more frequently than low fear-of-harm subjects (odds ratio, estimated by ordinal logistic regression modeling methods, was 2.42 (95% CI 2.00 to 2.92; $z=9.12$, $p<0.001$).

Limitations: Child report data was not obtained; clinician diagnosis was not validated via research interview.

* Corresponding author. Juvenile Bipolar Research Foundation, 7 Whitney Street Extension, Westport, CT 06880, United States. Tel.: +1 203 226 2216; fax: +1 203 341 0496.

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

Conclusions: Obsessive fears about harm to self or others in a sample of children with a clinician-assigned diagnosis of bipolar disorder were found to be positively related to increased behavioral aggression towards self and others, as well as to frequent suicide threats.

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1. Introduction

Obsessive fear about harm to self or others is observed in several childhood psychiatric conditions, including obsessive–compulsive disorder, separation anxiety disorder, and bipolar disorder. For some young patients, fear of harm may reflect a low threshold for anxiety, or it may be associated with hallucinatory or delusional images. Some evidence suggests that in bipolar patients, fear of harm may result from misattribution of threat to neutral social cues. Bipolar adults have demonstrated impaired recognition of facial emotion (Lembke and Ketter, 2002), and bipolar youth have demonstrated a bias to misidentify faces as angry (McClure et al., 2003).

Clinical experience with bipolar youth suggests that those most anxious about harm coming to themselves or others are also physically and verbally aggressive. The current debate about the cardinal features of juvenile mania and its differentiation from other psychiatric disorders has placed strong emphasis on the relationship of anxiety and paranoia to aggressive behavior. A recently published report notes, “it is important that particular care be given to assessing anxiety and subtle forms of paranoia in children with irritable (hypo)mania or mixed episodes, especially those who exhibit aggressive behavior” (Leibenluft et al., 2003a,b). Others who have investigated the features of anxiety and aggression in childhood bipolar disorder concur (Dilsaver and Chen, 2003; Masi et al., 2004; Post et al., 2004).

In this study, we inquired whether bipolar children and adolescents with recurrent fears of harm were more behaviorally aggressive than those with fewer, less obsessive fears. Using an extensive, Internet-based data acquisition system established by the Juvenile Bipolar Research Foundation (JBRF, 2004), we obtained data on obsessive fears via parents’

responses on the Yale–Brown Obsessive Compulsive Scale [YBOCS] (Goodman et al., 1989), and on aggressive behaviors via parents’ responses on the Overt Aggression Scale [OAS] (Yudofsky et al., 1986). In this report, we summarize data on the relationship between parent-reported fear of harm and parent-reported aggressive behavior in children assigned a formal diagnosis of bipolar disorder by a clinician.

2. Methods

2.1. Data acquisition

The JBRF has established an extensive, Internet-based system for data acquisition on children clinically diagnosed with bipolar disorder (JBRF, 2004). Sample selection for this study was based on parent report that the child/adolescent had been diagnosed with bipolar disorder by a clinician in the community. All subjects were assessed using the YBOCS, the OAS, and the Child Bipolar Questionnaire [CBQ] (Papolos and Papolos, 2002), a 65-item Likert-scale instrument used to screen for juvenile-onset bipolar disorder.

2.2. Fear-of-harm index

A fear-of-harm index was calculated by summing 6 YBOCS items occurring at a frequency of “3” (“often”) or “4” (“very often or almost constantly”): [1] Fear might harm self; [2] Fear might harm others; [3] Fear harm might come to self; [4] Fear harm will come to others (may be because of something child did or did not do); [8] Fear will act on unwanted impulses (e.g., to stab a family member); [10] Fear will be responsible for something else terrible happening (e.g., fire, burglary, flood). The distribution of scores on this measure was distinctly biphasic. We used med-

ian-split to define meaningful subgroups contrasting high vs. low fear-of-harm. These two subgroups were compared on OAS subscales and OAS total score, as well as on the two most severe OAS items: [11] Mutilates self, causes deep cuts, bites that bleed, internal injury, fracture, loss of consciousness, loss of teeth; [15] Attacks others, causing severe physical injury (broken bones, deep lacerations, internal injury).

In addition, in order to assess possible connections between fear-of-harm and suicidality, we compared high and low fear-of-harm subjects on a CBQ item assessing suicide threats: [60] Has made clear threats of suicide. Parent-reported suicide threats rated “very often or almost constantly” were coded as present and those rated “never or hardly ever,” “sometimes,” or “often” were coded as not present.

2.3. Statistical methods

We contrasted rates of high fear-of-harm between males and females and correlated this measure with each of several count or continuous measures characterizing the study sample, including the number of psychotropic medicines, the number of psychiatric diagnoses reported, and the OAS total score, using generalized linear modeling methods with binomial family and logarithmic link, to obtain a risk ratio (RR) and its 95% confidence interval (95% CI) for each of these explanatory factors. We contrasted children identified by parents on the Overt Aggression Scale as having frequent episodes of (A) self-harm, or (B) attacks on other persons, on three dimensions: males vs. females, older children (age >10) vs. younger, and fear-of-harm high vs. not-high. In these contrasts, risk ratios and their 95% CIs were obtained, using generalized linear modeling methods. We contrasted parental report of frequency of suicidal threats (CBQ Item 60) between high vs. low fear-of-harm subgroups, using $\chi^2[df=3]$ methods, and we obtained an adjusted odds ratio assessing the strength of the association between frequency of suicidal threats and high vs. low fear-of-harm indicator using ordinal logistic regression modeling methods. Model fits were checked using graphical methods. Robust standard error estimates were made when feasible. Averaged continuous data are reported as means with standard deviations (\pm SD) or 95% CIs. Statistical significance required 2-tailed $p < 0.05$. Analyses

employed commercial microcomputer programs (Stata®, Stata Corp., College Station, TX).

3. Results

There were 2262 subjects for whom both YBOCS and OAS data were obtained via the JBRF Internet-based system. 1601 (70.8%) of these children had been formally assigned a diagnosis of bipolar disorder by a clinician (i.e., child psychiatrist, psychiatrist, pediatrician, or other clinician), according to their parents. They comprised the study group for this report. 617 (37.3%) scored in the high fear-of-harm subgroup and 1039 (62.7%) scored in the low fear-of-harm subgroup. 425 (68.9%) of the high fear-of-harm subgroup were male vs. 629 (60.5%) of the low fear-of-harm subgroup, ($p = .001$). The average age of the high fear-of-harm subgroup was 10.6 years \pm 3.3 (2–18) vs. 11.4 years \pm 3.7 (2–20) for the low fear-of-harm subgroup, ($p < .001$). The average number of psychotropic medicines prescribed to the high fear-of-harm subgroup was 2.41 \pm 1.6 (0–18, $n = 327$); the average number prescribed to the low fear-of-harm subgroup was 2.21 \pm 1.4 (0–10, $n = 576$), ($p = .060$). The average number of psychiatric diagnoses given to the high fear-of-harm subgroup was 3.35 \pm 2.1 (0–9, $n = 327$); the average number given to the low fear-of-harm subgroup was 2.75 \pm 1.8 (0–9, $n = 576$), ($p < .001$).

3.1. OAS and YBOCS measures

There was a very large difference between the two fear-of-harm subgroups on average OAS total score (11.8 \pm 3.5 vs. 8.80 \pm 4.8), with a difference at the mean of more than 34%. Summary data on the most severe OAS item measures of harms-self (Item 11) and harms-others (Item 15) are provided in Table 1. These data indicate that children/adolescents identified as having high fear-of-harm anxieties were 2.7-fold (RR = 2.68) more likely to be identified by their parents as engaging in severely self-injurious behaviors than subjects with relatively low fear-of-harm anxieties; and these same children were 8-fold (RR = 7.97.4) more likely to be identified as engaging in severely injurious assaults on others. Older children were more likely to be identified by their parents/guardians as engaging in

Table 1

Characteristics of children reported by parents as Yes and No on Overt Aggression Scale items indicating severe symptoms of (A) self-harm or (B) attacks on other persons

Measure ^a	Yes on OAS item	No on OAS item	Risk ^b ratio	(95% CI) ^b	<i>z</i>	<i>p</i>
<i>A. OAS Item 11 (self-harm)^c</i>						
Number (%)	114 (7.1)	1487 (92.9)	–	–	–	–
Males	66/114 (57.9)	950/1487 (63.9)	0.79	0.55–1.13	–1.28	0.20
Age > 10 years	79/114 (69.3)	863/1477 (58.4)	1.56	1.06–2.29	2.25	0.025
Fear-of-harm > median	70/114 (61.4)	526/1487 (35.4)	2.68	1.87–3.86	5.32	<0.001
<i>B. OAS Item 15 (harm to others)^d</i>						
Number (%)	63 (3.9)	1538 (96.1)	–	–	–	–
Males	45/63 (71.4)	971/1538 (63.1)	1.44	0.84–2.46	1.33	0.18
Age > 10 years	29/63 (46.0)	913/1528 (59.8)	0.59	0.36–0.95	–2.15	0.032
Fear-of-harm > median	52/63 (82.5)	544/1538 (35.4)	7.97	4.19–15.2	6.33	<0.001

^a Fear-of-harm high vs. low subgroups defined by median-split on 6 YBOCS “fear-of-harm” items, together with YBOCS frequency ratings of at least 2 (often) on each of these 6 items.

^b Risk ratio and 95% CI estimated using generalized linear modeling (GLM) methods.

^c OAS Item 11: Mutilates self, causes deep cuts/bites that bleed, internal injury, fracture, loss of consciousness, loss of teeth. Current behavior rated Yes/No by parents/guardians.

^d OAS Item 15: Attacks others, causing severe physical injury (broken bones, deep lacerations, internal injury) mutilates self, causes deep cuts/bites that bleed, internal injury, fracture, loss of consciousness; rated Yes/No.

very severe self-harm behaviors, but younger children were more likely to be identified as engaging in severe harm-to-others behaviors.

The six YBOCS fear-of-harm items very strongly separate children and adolescents who were/were not

identified by their parents/guardians as actively engaging in severe harm-to-others behaviors. This is illustrated graphically in Fig. 1, which shows the count of the number of YBOCS fear-of-harm items endorsed by parents in relation to whether the child

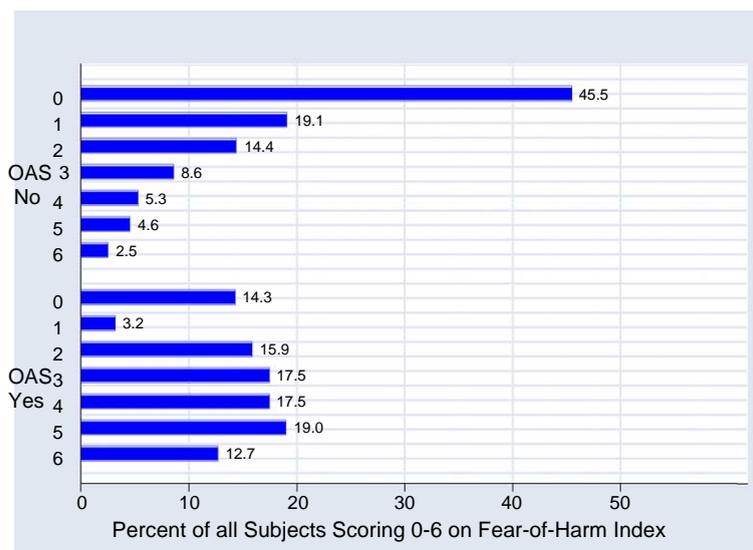


Fig. 1. Bar graph showing fear-of-harm index scores based on six YBOCS items for two subgroups: subjects scored as Yes vs. No on the Overt Aggression Scale “severe attacks on others” item. YBOCS-based fear-of-harm index is a count (0/6) of the number of items scored at a frequency of 3 (“very often or almost constantly”) or higher.

was/was not identified as exhibiting severe harm-to-others behaviors on OAS Item 15. The figure shows a very clear separation between subjects with/without overt harm-to-others behavioral patterns. In a small ($N=81$) healthy comparison group, these fear-of-harm–overt aggressive behavior correlations were near-zero.

3.2. Fear-of-harm and suicidality

YBOCS and CBQ data were available for 1696 subjects. Parents of the high fear-of-harm children/adolescents ($N=617$, 37.3%) were much more likely to report that their children frequently threatened suicide on CBQ Item 60 (“Has made clear threats of suicide”) than parents of the remaining subjects ($N=1039$). Fully one-quarter (27.2%) of the parents of the high fear-of-harm subjects indicated that their sons/daughters made clear threats of suicide with frequency “very often or almost constantly.” This percentage was more than twice the corresponding percentage among all other parents providing both YBOCS data and suicide threat (CBQ Item 60) data. When examined using ordered logistic regression modeling methods, the estimated odds ratio was 2.42 (95% CI 2.00 to 2.92; $z=9.12$, $p<0.001$).

4. Discussion

In this study, we examined the hypothesis that recurrent, intense fears about harm to self or others in a sample of children diagnosed with bipolar disorder by clinicians in the community would be positively related to aggressive acts directed towards self and others. We found that, in this sample, many parents reported that their children/adolescents had both persistent and morbid fear-of-harm anxieties and severe overt aggressive behaviors. In addition, parents of children/adolescents with high fear-of-harm were much more likely to report that their children made frequent suicide threats.

4.1. Age and sex associations with aggressive behavior

The fairly strong association between age and target of aggressive behavior is worthy of note. The

parents of the younger children in the study sample reported that the target of aggressive behaviors was more likely to be other children rather than self, a pattern reversed in the report of parents of older children. These data may reflect socialization processes resulting in the child’s redirecting aggression toward the self away from other children (presumably due to intervention by parents/teachers and other adults). However, because the study data are cross-sectional only, we cannot determine whether such a target-shift-with-age occurred in these children/adolescents.

The lack of association between sex and parent report of frequent and intense aggressive behaviors, either directed towards self or towards others, was somewhat contrary to expectation. We had expected that girls would be more likely to be reported to engage in aggressive acts towards self and boys more likely to be reported to direct aggressive acts towards others. In fact, neither expectation was supported in the data.

4.2. Clinical implications

If replicated, these findings may have important implications for the diagnosis and treatment of juvenile-onset bipolar disorder. A strong relationship between obsessive fear-of-harm and overt aggressive behavior could represent a potentially useful phenomenological feature of the disorder. The prescription of antidepressant medication, otherwise appropriate to treat obsessive fears, may be reconsidered for an intensely fearful, aggressive child with abrupt, rapid mood changes, in light of recent evidence of possible induction of manic symptoms, psychosis, or exacerbation of aggressive behavior (Faedda et al., 2004). Suicide risk might be closely monitored in such children.

4.3. Research implications

For researchers, the relationship between fear-of-harm and aggression may generate hypotheses about the neurobiological underpinnings of juvenile-onset bipolar disorder. Recent findings suggest that the perception of a fearful signal and its differentiation from a new, but emotionally content-free stimulus is affected by cortico-amygdala and autonomic activity

(Williams et al., 2004). Studies using positron-emission tomography (PET) and functional magnetic resonance imaging (fMRI) in humans have provided evidence that the amygdala, implicated in impaired fear conditioning, responds to social cues, such as angry and fearful facial expressions, perhaps more strongly, in fact, than to fearful situations or events (Morris et al., 1996; Hariri et al., 2002, 2003). Facial expressions of fear and anger have been found to result in significant increases in amygdala activity, even when the faces are unattended or presented briefly and masked (Bishop et al., 2004). Subtle anomalies in a neural circuit encompassing the amygdala may predispose to perturbed encoding of fearful faces and the inability to correctly process and respond to novel stimuli, including, and perhaps most importantly, social cues. Bipolar subjects may be especially vulnerable to this impairment.

4.4. Study limitations

Child report data using the CYBOCS, which has developmental adaptations generally deemed more appropriate for children, would have strengthened this report, as parents in general do not report as accurately on their children's internalizing behaviors. However, the practicality of assembling child report data from children of a wide range in age and from a sample size equivalent to the one reported here has been a thorny issue for many researchers. Similarly, clinician diagnoses, possibly influenced by the presentation of aggressive behavior, have not yet been adequately validated using conventional research diagnostic methods. The effort to address these limitations, 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.

4.5. Summary

We report a very strong relationship between parent-reported obsessive fear of harm and parent-reported aggressive behavior and frequent suicide threats in children diagnosed with bipolar disorder by a clinician. We believe that this initial evidence of a possible phenomenological feature of pediatric bipolar disorder warrants further research.

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