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## Is bipolar disorder specifically associated with aggression?

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### Abstract

**Objective**—Several studies have suggested that bipolar disorder (BP) in adults is associated with aggressive behaviors. However, most studies have only included inpatients and have not taken possible confounding factors into consideration. The goal of this study was to compare the prevalence of aggression in subjects with BP compared to subjects with other non-BP psychopathology and healthy controls.

**Methods**—Subjects with bipolar I disorder (BP-I) and bipolar II disorder (BP-II) (n = 255), non-BP psychopathology (n = 85), and healthy controls (n = 84) were recruited. Aggression was measured using the Aggression Questionnaire (AQ). Group comparisons were adjusted for demographic and clinical differences (e.g., comorbid disorders) and multiple comparisons. The effects of the subtype of BP, current versus past episode, polarity of current episode, psychosis, the presence of irritable mania/hypomania only, and pharmacological treatment were examined.

**Results**—Subjects with BP showed significantly higher total and subscale AQ scores (raw and *T*-scores) when compared with subjects with non-BP psychopathology and healthy controls. Exclusion of subjects with current mood episodes and those with common comorbid disorders yielded similar results. There were no effects of BP subtype, polarity of the current episode, irritable manic/hypomanic episodes only, or current use of pharmacological treatments. Independent of the severity of BP and polarity of the episode, those in a current mood episode showed significantly higher AQ scores than those not in a current mood episode. Subjects with current psychosis showed significantly higher total AQ score, hostility, and anger than those without current psychosis.

**Conclusions**—Subjects with BP display greater rates of anger and aggressive behaviors, especially during acute and psychotic episodes. Early identification and management of these behaviors is warranted.

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## Keywords

aggression; Aggression Questionnaire; anger; bipolar disorder; irritability

Bipolar disorder (BP) is a devastating psychiatric disorder, ranked by the World Health Organization among the top 10 disabling disorders in the world, with a prevalence of about 1% for bipolar I disorder (BP-I) and 3.0% to 8.3% for the bipolar spectrum disorders [BP-I, bipolar II disorder (BP-II), cyclothymia] (1).

BP has been associated with violent behaviors, particularly during mania, mixed episodes, or psychotic states (2). However, there are few studies regarding the prevalence of violent or aggressive behaviors in individuals with BP, and most of the existing studies include inpatient or penitentiary populations, thus limiting the generalizability of the results. For example, Barlow and colleagues (3) found in a sample of psychiatric inpatients ( $n = 1,269$ ) that patients with BP had more aggressive behaviors than patients with other Axis-I disorders [odds ratio (OR) = 2.81]. In contrast, Biancosino and colleagues (4) in a sample of 1,324 inpatients reported that physical assault was equally prevalent in patients with BP, schizophrenia, substance/alcohol abuse, and organic disorders. There is only one study in which anger and aggression were evaluated in a sample of adult outpatients (5). In that study, major depressive disorder (MDD), BP-I, intermittent explosive disorder, and cluster B personality disorders were associated with increased anger when compared to the other psychiatric disorders. Finally, a recent meta-analysis found that people with BP had significantly more violent behaviors than healthy controls [OR: 4.1, 95% confidence interval (CI): 2.9–5.8] (6). However, there was high heterogeneity in the subjects included in the studies and the methodology used to ascertain the violent behaviors.

Epidemiological studies evaluating the prevalence of severe violent behaviors in adults with psychiatric disorders may indirectly shed some light on the question of whether individuals with BP are more prone to aggression than individuals with other disorders. The National Comorbidity Survey showed that the 12-month adult population prevalence of violent behaviors was 2%, whereas it was 16% for adults with BP (7). With the exception of substance use disorder (SUD) (19%), the prevalence of violent behavior in adults with BP was higher than in adults with MDD, posttraumatic stress disorder (PTSD), or panic disorder (PD). The National Epidemiologic Survey on Alcohol and Related Conditions found a lifetime prevalence of violent behaviors of 0.66% in the general adult population (8). Again, with the exception of SUD (6%), the prevalence of violent behaviors was higher in subjects with BP (BP-I = 2.5% and BP-II = 5.1%). There was no information for schizophrenia or psychosis. The above results are limited because these studies ascertained aggressive behaviors using yes/no questions without considering the severity of the violent behaviors; therefore, a subject could be classified as violent by responding positively to just one of the items.

It is crucial to understand the relationship between BP and violent or aggressive behaviors because these behaviors are associated with increased risk for individual and familial suffering, socioeconomic and legal problems. Furthermore, they are a source of stigma and discrimination against people with psychiatric disorders (7). The aim of this study was to evaluate the prevalence of lifetime aggression in a sample of adult outpatients with BP as compared to a sample of community controls with and without non-BP psychopathology. We hypothesized that after adjusting for confounding factors such as comorbid Axis-I disorders and socioeconomic factors, lifetime aggression would be significantly higher in subjects with BP than in controls. In addition, we expected that among the subjects with BP, aggression would be more prevalent in those with a current mood episode, especially in

those subjects with a current manic/mixed episode, and in those with more severe current mood symptomatology.

## Methods

### Subjects

Subjects were recruited as part of the National Institute of Mental Health (NIMH) Pittsburgh Bipolar Offspring Study (BIOS) (9), which aims to evaluate the lifetime prevalence of psychiatric disorders in offspring of parents with BP. Briefly, adults with BP were recruited through advertisement, adult BP studies, and outpatient clinics. Subjects were required to fulfill DSM-IV criteria for BP-I or BP-II (10). Exclusion criteria were current or lifetime diagnoses of schizophrenia, mental retardation, mood disorders secondary to substance abuse, medical conditions, medication use, and living more than 200 miles away from Pittsburgh, PA, USA. Control subjects were recruited from the community by the University Center for Social and Urban Research, University of Pittsburgh, at a ratio of one control adult to two adults with BP. Control subjects were group matched by age, sex, and neighborhood using the area code and the first three digits of the telephone number of the subjects with BP. The exclusion criteria were the same as those for the subjects with BP, with an additional exclusion criterion of any lifetime or current BP and/or history of BP in first-degree relatives.

A sample of 255 subjects with BP, 85 subjects with any non-BP psychopathology, and 84 healthy controls ( $n = 84$ ) was recruited. As shown in Table 1, there were significant group differences in demographic factors. Caucasians were more highly represented among the BP sample, and subjects with BP were less likely to be married than the other two groups. Also, subjects with BP and non-BP psychopathology had lower socioeconomic status (SES) than the healthy controls (for all above noted comparisons  $p$ -values  $< 0.001$ ).

### Assessment

After Institutional Review Board approval and informed consent were obtained, subjects were assessed for psychopathology, family history of psychiatric disorders and other variables such as psychosocial functioning, family environment and exposure to negative life events. Only instruments relevant to this article are included.

Axis-I disorders, type and severity of current mood episode, presence of only irritable, only euphoric, or irritable/euphoric current and past manic/hypomanic episodes were evaluated using the DSM-IV Structured Clinical Interview (SCID) (11) plus the attention-deficit hyperactivity disorder (ADHD), disruptive behavior disorder (DBD), and the separation anxiety disorder (SAD) sections from the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children—present and lifetime version (K-SADS-PL) (12). Overall functioning was evaluated using the DSM-IV Global Assessment of Functioning (GAF) (10). Current and past pharmacological and psychosocial treatments were ascertained using the Adult Health Medical Screening Interview developed for BIOS. SES was evaluated using the four-factor Hollingshead Scale (13). All assessments were completed by bachelors- or masters-level interviewers with at least two years of experience and were carried out in the subjects' homes. All assessments were presented to a psychiatrist who was blind to the psychiatric status of the subjects. The overall SCID and KSADS kappas for all psychiatric disorders were 0.8.

Lifetime aggression was evaluated through the Aggression Questionnaire (AQ) (14). The AQ is an updated version of the classic Buss-Durkee Hostility Inventory (15), a widely known instrument for assessing lifetime anger and aggression. The internal consistency estimate of the AQ is 0.94 and the AQ has a strong construct and discriminant validity (16).

The AQ includes 34 likert-type items scored on five subscales: Physical Aggression (PHY), Verbal Aggression (VER), Anger (ANG), Hostility (HOS), and Indirect Aggression (IND). The PHY subscale includes items focused on the use of physical force when expressing anger: *'I may hit someone if he or she provokes me.'* The VER subscale is formed by items that make reference to hostile speech: *'When people annoy me, I may tell them what I think of them.'* The items of the ANG subscale describe aspects of anger related to arousal and sense of control: *'At times I feel like a bomb ready to explode.'* The HOS subscale refers to attitudes of social alienation and paranoia: *'I wonder what people want when they are nice to me.'* Finally, the IND subscale measures the tendency to express anger in actions that avoid direct confrontation: *'When someone really irritates me, I might give him/her the silent treatment.'*

Each of the items describe a characteristic related to aggression, and the individual rates the description on a scale from 1 (*Not at all like me*) to 5 (*Completely like me*), to form an AQ total score along with an inconsistent responding (INC) index score as a validity indicator. The INC is based on several pairs of items for which responses tend to be similar among individuals, for example: *'If somebody hits me, I hit back,'* and *'If I have to resort to violence to protect my rights, I will.'* If the difference scores between these pairs is bigger than one point, then the INC scores increases one point. The authors suggest questioning the accuracy of the individual's AQ response when the INC is  $\geq 5$ .

Total and subscale AQ scores can be reported as raw or *T*-scores. The *T*-norms were standardized in a sample of more than 2,000 individuals, aged 9–88, considered as representative of the USA population. The *T*-scores can be subdivided into various severity of aggression thresholds according to the following cut-off scores:  $\leq 29$ : *very low*; 30–39: *low*; 40–44: *low average*; 45–55: *average*; 56–59: *high average*; 60–69: *high*; and  $\geq 70$ : *very high* (16).

### Statistical analyses

Demographic and clinical characteristics among the groups were compared using  $\chi^2$ , ANOVA, and nonparametric tests as appropriate. Since the AQ subscales were significantly correlated (0.57 to 0.75), the raw and *T*-scores on each of the subscales were compared using MANOVA tests. ANCOVA models were built for group comparisons for raw and *T*-AQ total score and of each AQ subscale individually. These models were constructed in a hierarchical manner adjusting for any between-group demographic and clinical differences. Interactions were evaluated and included in the models if significant. Multinomial regression models were used to compare the different AQ *T*-thresholds.

Within the BP group, specific factors of interest were investigated using ANOVA tests: the BP type (BP-I/BP-II), the occurrence of mood episode (current, if the mood symptoms were present within a month before completing the scale versus past), the presence of current and/or past only irritable, only euphoric or irritable/euphoric manic/hypomanic episodes, the polarity of the current mood episode [manic/mixed, hypomanic, depressed and not otherwise specified (NOS)], the severity of the current mood episode (mild, moderate, severe), and the current exposure to pharmacological treatments (antidepressants, antipsychotics, stimulants, mood stabilizers). All pair-wise comparisons were corrected using the Bonferroni method. All continuous variables were reported as mean  $\pm$  standard deviations, and all *p*-values were based on two-tailed tests with  $\alpha = 0.05$ .

### Results

As shown in Table 2, subjects with BP had significantly higher lifetime prevalence of ADHD, DBD, SUD, PD, generalized anxiety disorder (GAD), PTSD, obsessive compulsive

disorder (OCD), and eating disorders (ED) when compared to the non-BP group (all  $p$ -values  $< 0.05$ ). Nineteen percent of adults with bipolar disorder had current only irritable manic/hypomanic episodes, 51% only euphoric and 30% irritable/euphoric. Similar rates were found for past manic/hypomanic episodes.

After adjusting for between group demographic and clinical differences (e.g., comorbid disorders) and multiple comparisons, subjects with BP showed significantly lower current and most severe past GAF scores than subjects with other non-BP psychopathology and healthy controls (all  $p$ -values  $< 0.001$ ). Subjects with non-BP psychopathology also had lower current and worse past functioning than the healthy controls (all  $p$ -values  $< 0.001$ ). For the overall sample there was a significant negative correlation between AQ total score and overall past ( $\rho = -0.47$ ,  $p < 0.001$ ) and current ( $\rho = -0.61$ ,  $p < 0.001$ ) functioning. There were no between-group differences in the correlations between total AQ score and GAF (all  $p$ -values  $> 0.08$ ).

### AQ raw scores

As depicted in Table 3, subjects with BP showed significantly higher scores on the total score and all of the subscales of the AQ when compared to subjects with non-BP psychopathology and healthy controls (all  $p$ -values  $< 0.001$ ). Subjects with non-BP psychopathology also had significantly higher scores on all the scales when compared to the healthy controls. Adjusting for significant between group demographic variables and multiple comparisons yielded similar results.

After adjusting for between group differences in ADHD, any anxiety disorders, DBD, and SUD, subjects with BP continued to show significantly higher total and each subscale AQ scores than the subjects with non-BP psychopathology (all  $p$ -values  $< 0.001$ ). As expected, after these adjustments there were no differences between the non-BP subjects and the healthy controls.

In addition to the above regressions, sensitivity analyses were done individually excluding ADHD, DBD, anxiety, and SUD, and adjusting for demographic and clinical differences and multiple comparisons. Excluding subjects with ADHD yielded the same results. Also, excluding DBD, anxiety and SUD with very few exceptions, yielded the same results, e.g., no between group differences in the physical aggression subscale after excluding subjects with anxiety or DBD.

The above-noted analyses were repeated excluding subjects with an AQ INC  $\geq 5$  (BP = 36, non-BP psychopathology = 10, healthy controls = 0). These analyses yielded identical results.

There were no statistical differences in the total AQ and each subscale between subjects with current only irritable, only euphoric, or euphoric/irritable manic/hypomanic episodes. In contrast, subjects with past only irritable manic/hypomanic episodes had significantly higher scores in the total AQ and in the verbal and anger subscales compared to those subjects with past only euphoric or euphoric/irritable episodes (results not shown; all  $p$ -values  $< 0.05$ ). Excluding subjects with only irritable past episodes yielded similar results to the ones noted above.

As shown in Table 4, BP subjects with a current episode had significantly higher scores on the total AQ score and all its subscales when compared to those BP subjects not in a current episode (all  $p$ -values  $< 0.001$ ). Adjusting for between-group demographic and clinical differences and current use of medications yielded similar results (all  $p$ -values  $< 0.05$ ). Among BP subjects in a current episode, there were no effects of the polarity (e.g.,

hypomanic, manic/mixed, depressed, NOS), or the severity (mild, moderate, severe) of the episodes on the AQ scores. However, subjects with current psychotic symptoms showed significantly higher total, anger and hostility AQ scores when compared to subjects without current psychotic symptoms (all  $p$ -values  $< 0.05$ , data not shown).

Finally, since there were AQ differences between BP subjects based on current episode, all above analyses were repeated only comparing subjects with BP not currently in-episode with subjects with non-BP psychopathology and healthy controls. Again, and after controlling for significant demographic and clinical differences and multiple comparisons, BP subjects not in a current episode showed significantly higher total and every AQ subscale scores than the other two groups (all  $p$ -values  $< 0.05$ ).

### AQ T-scores

As depicted in Figure 1, after adjusting for clinical and demographic differences and multiple comparisons, subjects with BP had significantly AQ total and each subscale scores 56 than subjects with non-BP psychopathology and the healthy controls (all  $p$ -values 0.001). Also, with the exception of the anger and hostility subscale, subjects with non-BP psychopathology had significantly greater total AQ and each subscale scores 56 when compared to healthy controls (all  $p$ -values  $< 0.05$ ).

### Discussion

To our knowledge, this is the first study evaluating aggression in adults with BP in comparison with adults with non-BP psychopathology and healthy controls. In summary, after adjusting for between group demographic and clinical differences (e.g., comorbid disorders), in comparison with adults with non-BP psychopathology and healthy controls, adults with BP showed significantly higher scores on the AQ total and each of the subscale raw and  $T$ -scores. Among adults with BP, independent of the severity of BP, the presence of only irritable manic/hypomanic episodes, and polarity of the current mood episode, those with current mood episodes showed significantly higher scores in AQ total and each of the subscale scores than those subjects not in a current mood episode. However, current mood symptomatology by itself did not completely account for the results because similar findings were obtained after excluding subjects in current mood episodes. Subjects with current psychosis showed significantly higher lifetime aggression levels than those without current psychosis in the AQ total and in the hostility and anger subscales. An analysis of the different types of medications that at least in theory could stabilize (antipsychotics and mood stabilizers) or destabilize (antidepressants and stimulants) subjects with BP, did not show any effects on the aggression scores. Finally, subjects with BP had poorer current and past functioning than the other two groups. Independently of the group, for all subjects, aggression was negatively correlated with overall functioning.

Before discussing the noted results in more detail, it is important to highlight the limitations of this study. First, the sample was recruited through a high-risk for BP study (9) and as a consequence, the results may not be generalizable to other populations. However, taking into account the age and sex of the control subjects, the lifetime prevalence of psychiatric disorders in the whole sample was similar to that reported in the National Comorbidity Survey Replication study (17). Also, the rates of comorbid psychiatric disorders in subjects with BP in our sample were similar to those reported in the adult BP literature (7, 17, 18). Nevertheless, it is important to highlight that although we excluded subjects with obvious mental retardation, cognitive function was not formally evaluated. In addition, we did not evaluate the effects of personality disorders, and the prevalence of psychosis in our non-BP psychopathology group was low (2%). Second, the results presented here are cross-sectional. Currently the sample is being followed prospectively, which will allow us to

replicate the findings of this study longitudinally. Third, the information collected in this study was obtained only from subjects' self-evaluations and not from their relatives or from criminal reports. Thus, subjects could have under or over-reported their aggressive behaviors. However, this potential bias might affect not only patients with psychiatric problems, but also healthy controls. In fact, in a large community study of adults with psychiatric disorders and healthy controls, the tendency to over report aggression was not only present in adults with psychopathology but also in the controls (19). Finally, AQ only evaluates lifetime aggression, and not current aggressive behaviors. However, as noted above, despite that current mood episodes were associated with higher aggression scores, excluding subjects with current mood episodes yielded the same results.

Existing studies have also reported increased aggression and anger associated with BP in comparison with patients with non-BP psychopathology [(20); see review by Lavatolav (2)]. However, most of these studies have only focused on the presence of aggression in patients with BP who were in an acute episode. In our study, subjects with acute episodes also reported significantly higher levels of aggression than those not in an acute episode. However, higher scores on the total and each subscale of the AQ were also found in subjects not in current mood episodes, suggesting that those subjects with current mood symptoms may indeed be more aggressive. Alternatively, the current mood state may influence the person's self-evaluation and memories leading them to evaluate themselves as more aggressive than actually were (1). It is important to emphasize that comparison of our results with the literature needs to be taken with caution because of differences in methodology (e.g., definition, assessment, and timing of the aggression, severity of the illness, and inpatient versus outpatient status).

Except for the presence of psychosis, we did not find any effects of the subtype of BP and the polarity of the current episode (depression, mixed) on the severity of aggression. Similar findings were recently reported in another study of BP patients (6). In contrast, Graz and colleagues (21) in a sample of 1,561 subjects with mood disorders found a significantly higher rate of criminal behaviors and violent crimes in patients with mania when compared with patients with bipolar or unipolar depression. Although there are no other studies directly examining the effects of psychosis in aggression and BP, in general psychosis has been associated with increased risk for aggression in patients with diverse psychopathology (22). It is important to highlight that subjects with BP and current psychosis had higher scores on the subscales (anger and hostility) that, according to the AQ study, were more related to psychopathology (14).

A recent study using the child equivalent of the AQ, the Child's Hostility Inventory (23), evaluated the aggression, hostility, and irritability of the offspring of the BP parents included in this paper. This study showed that the offspring of BP parents had only significantly more hostility and irritability when compared with the children of the control parents (24). If replicated, these results emphasize the importance of early identification and treatment of subjects with BP before they develop aggressive behaviors.

In conclusion, independently of polarity, severity of mood episodes, the presence of only irritable manic/hypomanic episodes, and comorbidity, subjects with BP, particularly when acutely ill and psychotic, have more verbal and physical aggression, hostility and anger than subjects with non-BP psychopathology and healthy controls. However, it is important to emphasize that the above results do not mean that subjects with BP are more prone to severe violent behaviors. In fact, the AQ does not measure severe violent behaviors such as homicide, rape or the use of weapons. Moreover, a recent large epidemiological study comparing community controls to patients with BP who had at least two inpatient admissions showed that patients with BP had more violent behaviors (e.g., homicide,

assault, robbery, sexual offenses), but the results were mainly accounted for by the use of substances and not the BP per se (6). Therefore, it is important to early identify and implement treatments to help subjects with BP to cope and manage their aggressiveness, and prevent substance abuse and perhaps other comorbid disorders, to avoid the development of more severe aggressive behaviors.

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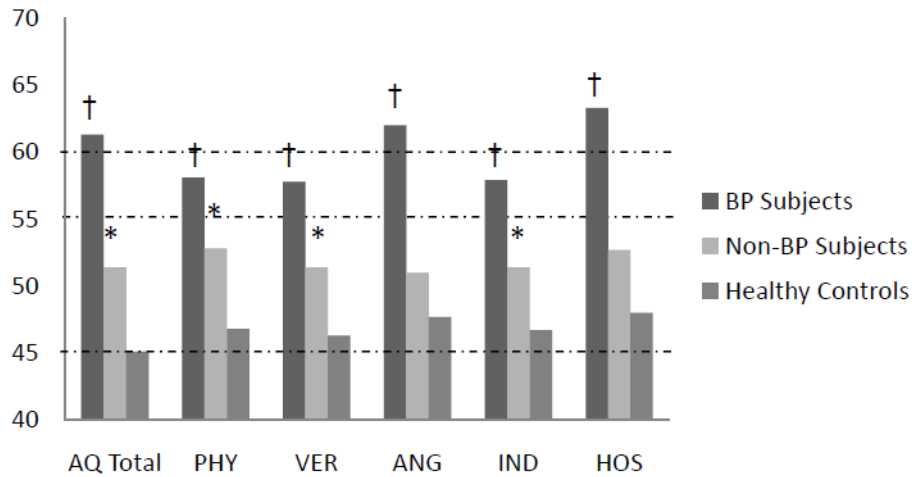
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## References

- Goodwin, FK.; Jamison, KR. Manic-depressive illness: bipolar disorders and recurrent depression. 2. New York: Oxford University Press; 2007.
- Latalova K. Bipolar disorder and aggression. *Int J Clin Pract.* 2009; 63:889–899. [PubMed: 19490199]
- Barlow K, Grenyer B, Ilkiw-Lavalle O. Prevalence and precipitants of aggression in psychiatric inpatient units. *Aust N Z J Psychiatry.* 2000; 34:967–974. [PubMed: 11127627]
- Biancosino B, Delmonte S, Grassi L, et al. Violent behavior in acute psychiatric inpatient facilities: a national survey in Italy. *J Nerv Ment Dis.* 2009; 197:772–782. [PubMed: 19829207]
- Posternak MA, Zimmerman M. Anger and aggression in psychiatric outpatients. *J Clin Psychiatry.* 2002; 63:665–672. [PubMed: 12197446]
- Fazel S, Lichtenstein P, Grann M, Goodwin GM, Langstrom N. Bipolar disorder and violent crime: new evidence from population-based longitudinal studies and systematic review. *Arch Gen Psychiatry.* 2010; 67:931–938. [PubMed: 20819987]
- Corrigan PW, Watson AC. Findings from the National Comorbidity Survey on the frequency of violent behavior in individuals with psychiatric disorders. *Psychiatry Res.* 2005; 136:153–162. [PubMed: 16125786]
- Pulay AJ, Dawson DA, Hasin DS, et al. Violent behavior and DSM-IV psychiatric disorders: results from the national epidemiologic survey on alcohol and related conditions. *J Clin Psychiatry.* 2008; 69:12–22. [PubMed: 18312033]
- Birmaher B, Axelson D, Monk K, et al. Lifetime psychiatric disorders in school-aged offspring of parents with bipolar disorder: the Pittsburgh Bipolar Offspring study. *Arch Gen Psychiatry.* 2009; 66:287–296. [PubMed: 19255378]
- Diagnostic and Statistical Manual of Mental Disorders. 4. Washington, D.C: American Psychiatric Association; 1994.
- First, MB.; Gibbon, M.; Spitzer, RL.; Williams, JBW. User's Guide for the Structured Clinical Interview for DSM-IV Axis-I Disorders Research Version (SCID-I, Version 2.0). New York: Biometrics Research, New York State Psychiatric Institute; 1996.
- Kaufman J, Birmaher B, Brent D, et al. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. *J Am Acad Child Adolesc Psychiatry.* 1997; 36:980–988. [PubMed: 9204677]
- Hollingshead, AB. Four-factor index of social status. New Haven: Yale University Sociology Department; 1975.
- Buss AH, Perry M. The aggression questionnaire. *J Pers Soc Psychol.* 1992; 63:452–459. [PubMed: 1403624]
- Buss AH, Durkee A. An inventory for assessing different kinds of hostility. *J Consult Psychol.* 1957; 21:343–349. [PubMed: 13463189]
- Buss, AH.; Warren, WL. Aggression Questionnaire. Western Psychological Services; 2000.



17. Merikangas KR, Akiskal HS, Angst J, et al. Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. *Arch Gen Psychiatry*. 2007; 64:543–552. [PubMed: 17485606]
18. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005; 62:593–602. [PubMed: 15939837]
19. Arseneault L, Moffitt TE, Caspi A, Taylor PJ, Silva PA. Mental disorders and violence in a total birth cohort: results from the Dunedin Study. *Arch Gen Psychiatry*. 2000; 57:979–986. [PubMed: 11015816]
20. Colasanti A, Natoli A, Moliterno D, Rossattini M, De Gaspari IF, Mauri MC. Psychiatric diagnosis and aggression before acute hospitalisation. *Eur Psychiatry*. 2008; 23:441–448. [PubMed: 18024087]
21. Graz C, Etschel E, Schoech H, Soyka M. Criminal behaviour and violent crimes in former inpatients with affective disorder. *J Affect Disord*. 2009; 117:98–103. [PubMed: 19168225]
22. Swanson JW, Swartz MS, Van Dorn RA, et al. A national study of violent behavior in persons with schizophrenia. *Arch Gen Psychiatry*. 2006; 63:490–499. [PubMed: 16651506]
23. Kazdin AE, Rodgers A, Colbus D, Siegel T. Children's Hostility Inventory: Measurement of aggression and hostility in psychiatric inpatient children. *J Clin Child Psychol*. 1987; 16:320–328.
24. Farchione TR, Birmaher B, Axelson D, et al. Aggression, hostility, and irritability in children at risk for bipolar disorder. *Bipolar Disord*. 2007; 9:496–503. [PubMed: 17680920]



**Fig. 1.**

Comparison of the Aggression Questionnaire (AQ) total and each subscale *T*-score among subjects with bipolar disorder (BP), non-BP psychopathology, and healthy controls. As per the normative data, ranges for *T*-scores were: 45–55 = normal; 56–59 = high average; 60–69 = high; and 70 = very high aggression (see dashed lines in figure). PHY = physical aggression; VER = verbal aggression; ANG = anger; IND = indirect subscale; HOS = hostility subscale.

\*\**p* < 0.001: comparisons between BP subjects versus non-BP psychopathology subjects and BP subjects versus healthy controls after adjusting for clinical and demographic differences, and multiple comparisons.

\**p* < 0.05: comparisons between non-BP psychopathology subjects and healthy controls after adjusting for clinical and demographic differences, and multiple comparisons.

Table 1

## Demographic characteristics

	BP (n = 255)	Non-BP (n = 85)	Healthy controls (n = 84)	Statistic	p-value
Age, years, mean (SD)	38.56 (7.80)	39.79 (8.80)	39.26 (7.50)	$F = 0.83$	0.43
Sex, female, %	79.2	80.0	76.0	$\chi^2 = 0.44$	0.8
Race, White, %	89.0 <sup>a</sup>	76.5 <sup>b</sup>	81.0 <sup>c</sup>	$\chi^2 = 9.11$	0.01
Marital status (% living together)	51.4 <sup>a</sup>	56.5 <sup>b</sup>	79.8 <sup>c</sup>	$\chi^2 = 21.01$	< 0.0001
SES, mean (SD)	34.94 (14.40) <sup>a</sup>	35.40 (13.00) <sup>a</sup>	40.36 (13.00) <sup>b</sup>	$F = 4.95$	0.007

BP = bipolar disorder; Non-BP = non-BP psychopathology; SD = standard deviation; SES = socioeconomic status.

<sup>a,b,c</sup> Different superscripts indicate significant differences among groups with p-values < 0.05 after Bonferroni's correction.

**Table 2**

Lifetime Axis-I psychiatric disorders for bipolar disorder (BP) and non-psychopathology (non-BP) subjects

	BP (n = 255)	Non-BP (n = 85)	Statistic	p-value
Bipolar I disorder	67.8	–	–	–
Bipolar II disorder	32.2	–	–	–
Major depressive disorder	–	44.7	–	–
Dysthymic disorder	–	11.7	–	–
Psychosis	1.6	2.4	Fisher's exact test	0.6
ADHD	25.9	8.2	$\chi^2 = 11.8$	0.0006
Disruptive behavior disorder	34.9	11.8	$\chi^2 = 16.5$	< 0.0001
ODD	26.7	7.1	$\chi^2 = 14.4$	< 0.0001
Conduct disorder	20.0	5.9	$\chi^2 = 9.2$	0.002
Substance use disorder	62.7	51.8	$\chi^2 = 3.2$	0.07
Alcohol	49.8	42.4	$\chi^2 = 1.4$	0.02
Drugs	42.4	25.9	$\chi^2 = 7.3$	0.007
Any anxiety	72.2	38.8	$\chi^2 = 30.7$	< 0.0001
Panic disorder	38.0	9.4	$\chi^2 = 24.5$	< 0.0001
SAD	9.0	9.4	$\chi^2 = 0.01$	0.9
GAD	27.5	4.7	$\chi^2 = 19.4$	< 0.0001
PTSD	36.5	18.8	$\chi^2 = 9.1$	0.003
OCD	13.7	2.4	$\chi^2 = 8.5$	0.004
Eating disorder	9.8	2.4	$\chi^2 = 4.8$	0.03

Values are reported as percent. ADHD = attention-deficit hyperactivity disorder; ODD = oppositional defiant disorder; SAD = separation anxiety disorder; GAD = generalized anxiety disorder; PTSD = posttraumatic stress disorder; OCD = obsessive compulsive disorder.

**Table 3**

Comparison of the Aggression Questionnaire (AQ) raw total and each subscale scores among subjects with bipolar disorder (BP), subjects with non-BP psychopathology (non-BP), and healthy controls

	<b>BP (n = 255)</b>	<b>Non-BP (n = 85)</b>	<b>Healthy controls (n = 84)</b>	<b>Statistics<sup>a,b</sup></b>
AQ total	87.93 ± 27.04 <sup>c</sup>	65.92 ± 21.58 <sup>d</sup>	54.15 ± 12.09 <sup>e</sup>	<i>F</i> = 75.4
Physical	17.36 ± 8.37 <sup>c</sup>	13.43 ± 5.77 <sup>d</sup>	10.81 ± 3.55 <sup>e</sup>	<i>F</i> = 29.9
Verbal	13.93 ± 5.35 <sup>c</sup>	11.01 ± 4.08 <sup>d</sup>	9.01 ± 2.65 <sup>e</sup>	<i>F</i> = 39.2
Anger	19.30 ± 6.03 <sup>c</sup>	14.37 ± 5.00 <sup>d</sup>	11.74 ± 3.14 <sup>e</sup>	<i>F</i> = 73.6
Hostility	22.50 ± 8.46 <sup>c</sup>	15.17 ± 6.40 <sup>d</sup>	12.58 ± 4.51 <sup>e</sup>	<i>F</i> = 70.8
Indirect	14.85 ± 4.94 <sup>c</sup>	11.93 ± 4.28 <sup>d</sup>	10.01 ± 2.87 <sup>e</sup>	<i>F</i> = 42.1

<sup>a</sup>All p-values < 0.001.

<sup>b</sup>All p-values < 0.001 when adjusted for marital status, race, and socioeconomic status.

<sup>c,d,e</sup>Different superscripts indicate significant differences among groups with p-values < 0.05, after Bonferroni's correction.

**Table 4**

Comparison of the Aggression Questionnaire (AQ) raw total and each subscale scores between subjects with current and past mood episodes

	Subjects with current BP episodes (n = 174)	Subjects with past BP episodes (n = 81)	p-value	p-value <sup>a</sup>
AQ total	93.8 ± 27.6	75.5 ± 24.1	< 0.001	0.001
Physical	18.6 ± 8.6	14.1 ± 6.3	< 0.001	0.01
Verbal	14.5 ± 5.3	12.2 ± 4.4	< 0.001	0.03
Anger	21.7 ± 6.8	17.1 ± 6.4	< 0.001	< 0.001
Hostility	23.7 ± 8.1	19.0 ± 7.9	< 0.001	0.006
Indirect	15.2 ± 4.8	13.2 ± 4.4	0.001	0.04

BP = bipolar disorder.

<sup>a</sup>Adjusted for age, anxiety, and disruptive behavior disorders.