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Original Article

Is bipolar disorder specifically associated with aggression?

Ballester J, Goldstein T, Goldstein B, Obreja M, Axelson D, Monk K, Hickey MB, Iyengar S, Farchione T, Kupfer DJ, Brent D, Birmaher B. Is bipolar disorder specifically associated with aggression? Bipolar Disord 2012: 14: 283–290. © 2012 The Authors. Journal compilation © 2012 John Wiley & Sons A/S.

Objective: Several studies have suggested that bipolar disorder (BP) in adults is associated with aggressive behaviors. However, most studies have included only inpatients and have not taken into consideration possible confounding factors. The goal of the present 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 to 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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Bipolar disorder (BP) is a devastating psychiatric disorder, ranked by the World Health Organization among the top ten disabling disorders in the world, with a prevalence of about 1% for bipolar I disorder (BP-I) and 3.0–8.3% 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]. By 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 an increased risk for individual and familial suffering, and socioeconomic and legal problems. Furthermore, they are a source of stigma and discrimination against people with psychiatric disorders (7). The aim of the present study was to evaluate the lifetime prevalence of 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 the 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, $p < 0.001$).

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

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
Gender, female,%	79.2	80.0	76.0	$\chi^2 = 0.44$	0.8
Race, white, %	89.0[a]	76.5[b]	81.0[c]	$\chi^2 = 9.11$	0.01
Marital status (% living together)	51.4[a]	56.5[b]	79.8[c]	$\chi^2 = 21.01$	< 0.0001
SES, mean (SD)	34.94 (14.40)[a]	35.40 (13.00)[a]	40.36 (13.00)[b]	$F = 4.95$	0.007

BP = bipolar disorder; Non-BP = non-BP psychopathology; SD = standard deviation; SES = socioeconomic status.
After Bonferroni's correction, means with different superscripts ([a,b,c]) indicate significant differences among groups (BP, non-BP, and healthy controls) with p-values ≤ 0.05.

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 Bachelor's or Master's degree-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 K-SADS-PL 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 describes 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 are larger than 1 point, then the INC scores increase by 1 point. The authors suggest questioning the accuracy of the individual's AQ response when the INC is ≥ 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 2000 individuals, aged 9–88, considered as representative of the US population. The *T*-scores can be subdivided into various severity of aggression thresholds according to the following cutoff scores: ≤ 29: *very low*; 30–39: *low*; 40–44: *low average*; 45–55: *average*; 56–59: *high average*; 60–69: *high*; and ≥ 70: *very high* (16).

Statistical analyses

Demographic and clinical characteristics among the groups were compared using χ^2, analysis of variance (ANOVA), and nonparametric tests as appropriate. Since the AQ subscales were significantly correlated (0.57–0.75), the raw and *T*-scores on each of the subscales were compared

using multivariate ANOVA tests. Analysis of covariance models were built for group comparisons for raw and *T*-AQ total score and for 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, antipsychotic agents, stimulants, mood stabilizers).

All pair-wise comparisons were corrected using the Bonferroni method. All continuous variables were reported as mean ± standard deviations, and all p-values were based on two-tailed tests with $\alpha = 0.05$.

Table 2. Lifetime Axis-I psychiatric disorders for bipolar disorder (BP) and non-BP 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	42.2	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 percentages. 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.

Results

As shown in Table 2, subjects with BP had a significantly higher lifetime prevalence of ADHD, DBD, 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 BP 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 individual 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.

Table 3. Comparison of the Aggression Questionnaire (AQ) raw total and individual subscale scores among subjects with bipolar disorder (BP), non-BP psychopathology (non-BP), and healthy controls

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

All p-values < 0.001 when adjusted for marital status, race, and socioeconomic status.
[a,b,c]Significant differences among groups ([a]BP group, [b]non-BP group, [c]healthy controls) with p-values ≤ 0.05, after Bonferroni's correction.

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. In addition, excluding DBD, anxiety, and SUD, with very few exceptions, yielded the same results (e.g., there were 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 ≥ 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 individual subscale scores between subjects with current only irritable, only euphoric, or euphoric/irritable manic/hypomanic episodes. By 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 those 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, neither the polarity (e.g., hypomanic, manic/mixed, depressed, NOS) nor the severity (mild, moderate, severe) of the episodes had any effect 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).

Table 4. Comparison of the Aggression Questionnaire (AQ) raw total and individual 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[a]
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.
[a]Adjusted for age, anxiety, and disruptive behavior disorders.

Finally, since there were AQ differences between BP subjects based on current episode, all of the above analyses were repeated comparing only subjects with BP not in a current 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 individual 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 higher AQ total and individual subscale scores of ≥ 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).

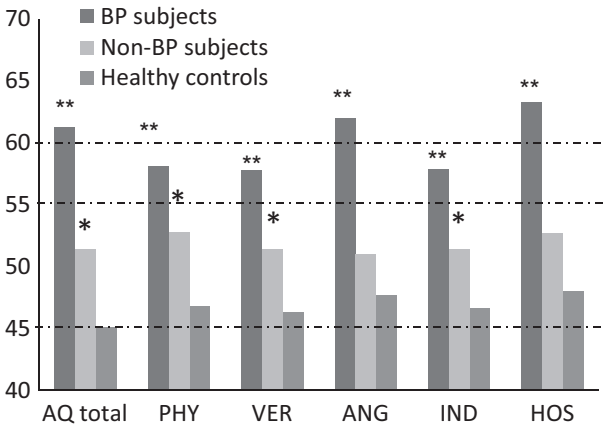

Fig. 1. Comparison of the Aggression Questionnaire (AQ) total and each subscale T-scores among subjects with bipolar disorder (BP), non-BP psychopathology, and healthy controls. ANG = anger; HOS = hostility subscale; IND = indirect subscale; PHY = physical aggression; VER = verbal aggression. As per the normative data, ranges for T-scores are: 45–55 = normal; 56–59 = high average; 60–69 = high; and ≥ 70 = very high aggression (see dashed lines above). *$p \leq 0.05$: comparisons between non-BP subjects and healthy controls after adjusting for clinical, demographic differences, and multiple comparisons. **$p \leq 0.001$: comparisons between BP subjects versus non-BP subjects and BP subjects versus healthy controls after adjusting for clinical, demographic differences, and multiple comparisons.

Discussion

To our knowledge, the present study was the first to evaluate aggression in adults with BP in comparison to adults with non-BP psychopathology and healthy controls. In summary, after adjusting for between-group demographic and clinical differences (e.g., comorbid disorders), adults with BP showed significantly higher scores on the AQ total and individual subscale raw and *T*-scores in comparison to adults with non-BP psychopathology and healthy controls. Among adults with BP, independent of the severity of BP, the presence of only irritable manic/hypomanic episodes, and the polarity of the current mood episode, those with current mood episodes showed significantly higher scores in AQ total and individual 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 the hostility and anger subscale scores. An analysis of the different types of medications that, at least in theory, could stabilize (antipsychotic agents 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. For all subjects, independent of their group, aggression was negatively correlated with overall functioning.

Before discussing these results in more detail, it is important to highlight the limitations of this study. First, the sample was recruited through a study comprising subjects at high risk for developing BP (9), so the results may not be generalizable to other populations. However, taking into account the age and gender 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). In addition, 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 overreported 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 overreport aggression was not only present in adults with psychopathology, but also in the controls (19). Finally, the AQ evaluates only lifetime aggression, and not current aggressive behaviors. However, as noted above, despite the fact that current mood episodes were associated with higher aggression scores, the exclusion of subjects with current mood episodes yielded the same results.

Existing studies have also reported increased aggression and anger in patients with BP in comparison to those with non-BP psychopathology (20) [see also review by Latalova (2)]. However, most of these studies have focused only on the presence of aggression in patients with BP who were

in an acute episode. In the present 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 individual subscales 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 they actually were (1). It is important to emphasize that a comparison between the present results and those in the literature should be interpreted with caution because of differences in methodology (e.g., the 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). By contrast, in a sample of 1561 subjects with mood disorders, Graz and colleagues (21) found a significantly higher rate of criminal behaviors and violent crimes in patients with mania when compared to patients with bipolar or unipolar depression. Although there have been no other studies directly examining the effects of psychosis in aggression and BP, in general psychosis has been associated with an increased risk of 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, which are closely related to psychopathology (14).

A recent study (24) 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. Farchione and colleagues showed that the only factors that were significantly increased in the offspring of BP parents compared to those of control parents were hostility and irritability (24).

In conclusion, subjects with BP, independently of polarity, severity of mood episodes, the presence of only irritable manic/hypomanic episodes, and comorbidity, and 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 had at least two inpatient admissions showed that although patients with BP had more violent behaviors (e.g., homicide, assault, robbery, sexual offenses), the results were in large part accounted for by the use of substances, and not the BP *per se* (6,25). Therefore, early identification and treatment of subjects with BP are important to help subjects with BP to manage their aggressiveness and prevent substance abuse and perhaps other comorbid disorders, and avoid the development of more severe aggressive behaviors.

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