



Research report

The impact of comorbid posttraumatic stress disorder on bipolar disorder patients

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ABSTRACT

Background: Available data regarding posttraumatic stress disorder (PTSD) in bipolar disorder (BD) are scarce and usually from a limited sample size. The present report was carried out using the Brazilian Research Consortium for Bipolar Disorders and aimed to examine whether patients with BD and comorbid PTSD are at an increased risk for worse clinical outcomes.

Methods: A consecutive sample of bipolar I outpatients from two teaching hospitals in Brazil was recruited. Patients were assessed using the Structured Clinical Interview for DSM-IV, Young Mania Rating Scale, 17-item Hamilton Rating Scale for Depression, and quality of life instrument WHOQOL-BREF. Participants were divided into three groups: a. bipolar patients with PTSD, b. bipolar patients exposed to trauma without PTSD, and c. bipolar patients with no trauma exposure.

Results: Of the 405 patients who consented to participate, 87.7% completed the survey. All three groups were similar in terms of demographic parameters. The group with comorbid PTSD reported worse quality of life, more rapid cycling, higher rates of suicide attempts, and a lower likelihood of staying recovered.

Limitations: The cross-sectional design excludes the opportunity to examine causal relationships among trauma, PTSD, and BD.

Conclusions: The findings indicate that PTSD causes bipolar patients to have a worse outcome, as assessed by their lower likelihood to recover, elevated proportion of rapid cycling periods, increased risk of suicide attempts, and worse quality of life.

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1. Introduction

Bipolar subjects are at high risk for experiencing traumatic events. This may be due to disruptive behavior during mania or increased childhood trauma (Brown et al., 2005; Goldberg and Garno, 2005; Romero et al., 2009). Consequently, patients with bipolar disorder (BD) usually report elevated rates of

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lifetime posttraumatic stress disorder (PTSD) ranging from 16% to 39% of bipolar I patients in the National Comorbidity Survey-Replication (OR 6.6, 95% CI 4.2–10.4) (Otto et al., 2004; Merikangas et al., 2007). Bipolar women (both I and II) are nearly twice as likely to have PTSD than bipolar men (20.9% vs. 10.6% in the STEP-BD study) (Baldassano et al., 2005 <http://www.springerlink.com/content/85772105ng582153/fulltext.html> - CR41), a finding similar to the ratio found in the general population (Kessler et al., 2005).

Furthermore, traumatic events that occur during manic or hypomanic episodes have a higher likelihood of inducing PTSD symptoms (Kennedy et al., 2002). Recent evidence suggests that a history of trauma may be related to both the etiology and the illness course of BD (Otto et al., 2004). Findings demonstrate that high-impact trauma (e.g., sexual abuse) has been associated with poor BD prognosis (Neria et al., 2002), and documentation has reported elevated rates of PTSD in patients with BD. Nonetheless, little is known about the quality of life (QOL) impairment and clinical impact imposed by PTSD on bipolar patients.

In this paper, we have used data gathered by the Brazilian Research Consortium on Bipolar Disorders to determine whether patients with comorbid PTSD have an increased risk for attempting suicide and whether they are more likely to experience more rapid cycling. Additionally, we have also explored the link between PTSD comorbidity and QOL impairment in those individuals. We have hypothesized that comorbid PTSD in BD would be associated with increased mood instability, more numerous suicide attempts, and more severely impaired QOL scores.

2. Methods

2.1. Subjects and clinical assessments

A sample of 405 consecutive bipolar I outpatients seeking treatment at the Bipolar Disorder Program, Hospital de Clínicas, Federal University, Porto Alegre and at the teaching Hospital, Federal University, Bahia, Brazil, was invited to participate. Eligible patients were older than 18 years of age and had confirmed BD diagnosis criteria according to the DSM-IV. The Institutional Review Boards of both sites approved the study protocol. After providing written informed consent, patients were evaluated in person through a socio-demographic history form to assess age, gender, marital status, and occupational status and through a clinical interview. Diagnoses were obtained by the Structured Clinical Interview for DSM-IV (SCID) I, a partly semi-structured interview for the DSM-IV (First et al., 1997). To assess depressive symptoms, the 17-item Hamilton Rating Scale for Depression (HAM-D-17) with a structured interview guide was used (Hamilton, 1960); to assess manic symptoms, the Young Mania Rating Scale (YMRS) was used (Young et al., 1978). All of the aforementioned measuring tools were translated into Portuguese.

2.2. Quality of life

Quality of life was assessed by an instrument termed the WHOQOL-BREF. It was developed by the World Health Organization and validated in several studies since its

development (WHOQOL Group, 1998). Apart from the first 2 items of general nature, the remaining 24 items of the instrument comprise four QOL domains denoted 'physical health', 'psychological', 'social relationships', and 'environment'. The four domain scores denote an individual's perception of QOL in each particular domain. Domain scores are scaled in a positive direction (i.e., higher scores denote a higher QOL).

2.3. Statistical analysis

We divided the participants into three groups: BD patients with PTSD (BD-PTSD), bipolar patients exposed to trauma but without PTSD (BD-trauma), and BD patients with no PTSD or trauma exposure (BD-control). The three groups were compared with regard to demographic and clinical data. A one-way between-groups analysis of variance, followed by the post-hoc Tukey test, was used to sort the three groups by age, and the Mann-Whitney test was used to analyze the continuous variables. Categorical variables were tested by the Pearson chi-squared test. These variables were considered valid on the condition that more than 80% of the cells had expected counts above five. Fisher's Exact Test was used to compare two dichotomous variables. All tests were carried out using a significance level of 5% (p -value $\leq .05$).

In bivariate and multivariate analyses, the Poisson regression with robust variance estimate was used to obtain the prevalence ratios (PR) between-groups BD-trauma vs. BD-control and BD-PTSD vs. BD-control to identify the number of suicide attempts. The Poisson multivariate model was adjusted for gender, age, marital status, occupational status, psychotic features at the first mood episode, and mood status (mania, depression, mixed state, and hypomania) at the first episode. The criterion that variables were considered to be possible confounders was if they caused a proportional difference between the crude and adjusted association measurements higher than 10% ($\Delta\% \geq 10$). In all analyses, prevalence ratio and 95% confidence intervals (CIs) were reported.

To explore whether trauma history or PTSD comorbidity is associated with mood instability, we conducted a logistic multivariate model with each group (2 = BD-PTSD, 1 = BD-trauma, 0 = BD-control) as the predictor and rapid cycling presence (1 = present, 0 = absent) as the outcome. We then adjusted these analyses for a set of potential confounders that we defined as background variables (Table 1). Variables that were considered to be possible confounders ($\Delta\% \geq 10$) were assessed by a multivariable model. In all analyses, PR and 95% CI were reported.

To test whether either trauma history or PTSD increases the risk of QOL impairment and more severe manic or depressive current symptoms among patients with BD, we conducted a series of linear regression models with robust variance estimate for trauma and PTSD comorbidity as the predictors and the WHOQOL-BREF domains (YMRS and HAM-D-17) as the outcomes, according to the difference of means between groups. Variables that were considered to be possible confounders ($\Delta\% \geq 10$) were assessed by a multivariate model. All statistical analyses were performed with the statistical software package STATA (version 9.0), using a significance level of 5% (p -value $\leq .05$).

Table 1
Patient demographics and clinical characteristics.

	BD-control (N = 254)	BD-trauma (N = 60)	BD-PTSD (N = 40)	Test (df); p value
Characteristics				
Age in years (SD)	41.2 (12.22)	41.32 (12.46)	39.67 (10.05)	*.32
Gender				
Female % (N)	66.9 (170)	73.3 (44)	85 (34)	** (2) = 5.74; .056
Male % (N)	33.1 (84)	26.7 (16)	15 (6)	
Marital status				
Single % (N)	40.6 (102)	23.3 (14)	28.2 (11)	** (6) = 12.08; .56
Married % (N)	34.3 (86)	35 (21)	41 (16)	
Separated/divorced % (N)	19.9 (50)	28.3 (17)	25.6 (10)	
Widowed % (N)	5.2 (13)	13.3 (8)	5.1 (2)	
Occupational status				
Paid activity (yes) % (N)	58.9 (146)	77.2 (44)	60.5 (23)	** (2) = 6.65; .036
Psychosis at first episode % (N)	(53.6) 131	44.1 (26)	41.0 (16)	** (6) = 6.12; .41
Mood status at first episode				
Mania % (N)	41.5 (102)	27.1 (16)	20.5 (8)	** (8) = 12.61; .12
Depression % (N)	46.3 (114)	55.9 (33)	61.5 (24)	
Mixed state % (N)	6.1 (15)	13.6 (8)	10.3 (4)	
Hypomania % (N)	2.0 (5)	1.7 (1)	2.6 (1)	

SD = standard deviation; BD = bipolar disorder; PTSD = posttraumatic stress disorder.

*Mann-Whitney test; ** χ^2 (df) test; the df is degree of freedom (number of row – 1 × number of columns – 1).

3. Results

Of the 405 patients who consented to participate, 50 (12.3%) were excluded because of missing data; thus, 355 patients (87.7%) completed the survey. Participants had a mean age of 36.2 (SD 8.8 years) (ranging from 19 to 57) and were mostly female ($N = 248$, 69.8%). Most patients were single ($N = 127$, 35.8%) or married ($N = 123$, 34.6%). A minority of patients was either separated or divorced ($N = 77$, 21.7%) or widowed ($N = 23$, 6.5%). Demographics and clinical characteristics are presented in Table 1. The prevalence of positive screenings for trauma ($N = 100$, 28.2%) or comorbid PTSD ($N = 40$, 11.3%) did not vary significantly with gender, age, marital status, occupational status, psychotic features at the first mood episode, or mood status (mania, depression, mixed state, and hypomania) at the first episode.

BD trauma patients did not report an increased prevalence of rapid cycling PR = 1.13 (95% CI: 0.62–2.05). BD PTSD patients were 2.2 times more likely to report rapid cycling

moods than the control group PR = 2.22 (95% CI: 1.37–3.60) (Table 2). After adjusting for potential demographic and diagnostic confounders, however, only the statistical association with rapid cycling remained among these patients PR = 1.58 (95% CI: 0.94–2.67). Similarly, BD trauma patients were not significantly more likely to attempt suicide PR = 1.23 (95% CI: 0.94–1.61), whereas BD PTSD patients were significantly more likely to do so than the BD control group (OR) = 1.5; 95% CI: 1.13–2.0) (Table 2). After adjusting, though, BD PTSD patients demonstrated only a statistical trend toward increased suicide attempts (OR) = 1.31 (95% CI: 0.98–1.76) (Table 2).

Among patients screening positive for PTSD, significantly higher scores of manic symptoms were found in comparison to controls. This difference remained significant after adjustment for covariates. On the other hand, BD trauma patients showed lower depressive scores than controls did (Table 2).

Finally, QOL scores were worse for patients with PTSD comorbidity in the 'psychological' domain, 'social relationships' domain, and 'environment' domain (Table 3, Fig. 1).

Table 2
Number of lifetime suicide attempts and the presence of rapid cycling in the previous year for bipolar patients, by trauma and comorbid PTSD status.

	BD-control (N = 255)		BD-trauma (N = 60)		BD-control (N = 255)		BD-PTSD (N = 40)	
	Crude		Adjusted ^a		Crude		Adjusted ^a	
Number of suicide attempts								
Prevalence ratio (95% CI)	1.23 (0.94–1.61)	$p = 0.12$	1.06 (0.80–1.40)	$p = 0.69$	1.50 (1.13–2.00)	$p = 0.005$	1.31 (0.98–1.76)	$p = 0.072$
Rapid cycling %								
Prevalence ratio (95% CI)	1.13 (0.62–2.05)	$p = 0.69$	0.81 (0.45–1.44)	$p = 0.47$	2.22 (1.37–3.60)	$p = 0.001$	1.58 (0.94–2.67)	$p = 0.08$
	BD-control Mean (SD)	BD-trauma Mean (SD)	Crude mean difference (p)	Adjusted ^a mean difference (p)	BD-control Mean (SD)	BD-PTSD Mean (SD)	Crude mean difference (p)	Adjusted ^a mean difference (p)
YMRS mean (SD)	7.38 (7.08)	8.53 (5.92)	1.15 ($p = .02$)	0.12 ($p = 0.89$)	7.38 (7.08)	15.84 (9.42)	8.46 ($p = .000$)	7.2 ($p = .000$)
HAM-D-17	8.97 (12.48)	4.0 (4.75)	–4.97 ($p = .000$)	–3.22 ($p = 0.002$)	8.97 (12.48)	5.97 (8.36)	–2.99 ($p = .056$)	–1.39 ($p = .39$)

SD = standard deviation; BD = bipolar disorder; PTSD = posttraumatic stress disorder. p : p-value.

^a Adjusted for gender, age, marital status, occupational status, psychotic features at the first mood episode, and mood status (mania, depression, mixed state, and hypomania) at first episode.

Table 3

Quality of life status of bipolar patients with trauma and comorbid PTSD status.

WHOQOL domains ^a	BD-control (N=95) vs. BD-trauma (N=55)				BD-control (N=95) vs. BD-PTSD (N=30)			
			Crude difference	Adjusted ^b difference			Crude difference	Adjusted ^b difference
Physical health Mean (SD)	54.2 (19.54)	53.1 (20.11)	-1.1 (0.75)	1.65 (0.62)	54.2 (19.54)	45.8 (21.88)	8.4 (0.05)	-7.65 (0.07)
Psychological health Mean (SD)	54.2 (21.18)	53.6 (20.19)	-0.6 (0.88)	4.5 (0.15)	54.2 (21.18)	39.19 (16.92)	-15.01 (0.001)	-11.29 (0.002)
Social relations Mean (SD)	55.8 (22.66)	53.7 (22.83)	-2.1 (0.6)	0.10 (0.98)	55.8 (22.66)	41.7 (21.10)	-14.1 (0.002)	-12.56 (0.005)
Environment Mean (SD)	57 (16.29)	54.7 (15.19)	-2.3 (0.39)	0.29 (0.91)	57 (16.29)	47.6 (12.13)	-9.4 (0.001)	-7.52 (0.012)

SD = standard deviation; BD = bipolar disorder; PTSD = posttraumatic stress disorder.

^a Lower scores denote worse functioning.^b Adjusted for gender, age, marital status, occupational status, psychotic features at the first mood episode, and mood status (mania, depression, mixed state, and hypomania) at the first episode.

The group difference in WHOQOL-BREF scores remained statistically significant after adjustment for covariates of all domains except 'physical health' (items 1 and 7); both items in this domain showed only a statistical trend to be worse in the univariate than multivariate comparison.

4. Discussion

In this clinical sample of bipolar I patients, we found that 11% of these individuals had comorbid PTSD. This rate is lower than that found in the Systematic Treatment Enhancement Program for Bipolar Disorder (18.8%) for bipolar I (Simon et al., 2004), but it is almost twice as high as the one reported as the lifetime prevalence of PTSD in the general population by another study (Kessler et al., 1995). Our study adds to the literature by showing that the comorbidity of PTSD with BD is strongly associated with such negative clinical outcomes as mood instability, and impaired QOL, even after adjustment for demographic and clinical covariates. Independently, PTSD is a condition associated with a higher

risk for suicidal behavior. Mental health professionals must be vigilant for this behavior, especially in populations of bipolar individuals who are already at risk for suicide (Simon et al., 2007; Carballo et al., 2008). Our finding of a higher number of suicide attempts (up to 50% among BD-PTSD patients in comparison to bipolar controls) strongly corroborates the hypothesis that PTSD comorbidity represents an important risk factor for suicide attempts in BD.

Previous reports have demonstrated that higher rates of comorbidity with anxiety disorders, specifically with PTSD (Simon et al., 2004), are an important factor associated with poorer QOL among BD patients (Neria et al., 2008). Moreover, our results show consistent and significant QOL impairment in three of the four WHOQOL-BREF domains, and this impairment remains significant even after adjustment for covariates. In general, the impact of BD on QOL appears to be of a similar magnitude to the impact of chronic diseases (e.g., chronic renal disease or rheumatoid arthritis) (Gutiérrez-Rojas et al., 2008). Despite the fact that QOL scores are likely to be markedly more impaired in BD patients during the depressive phase (Dias et al., 2008), factors like manic

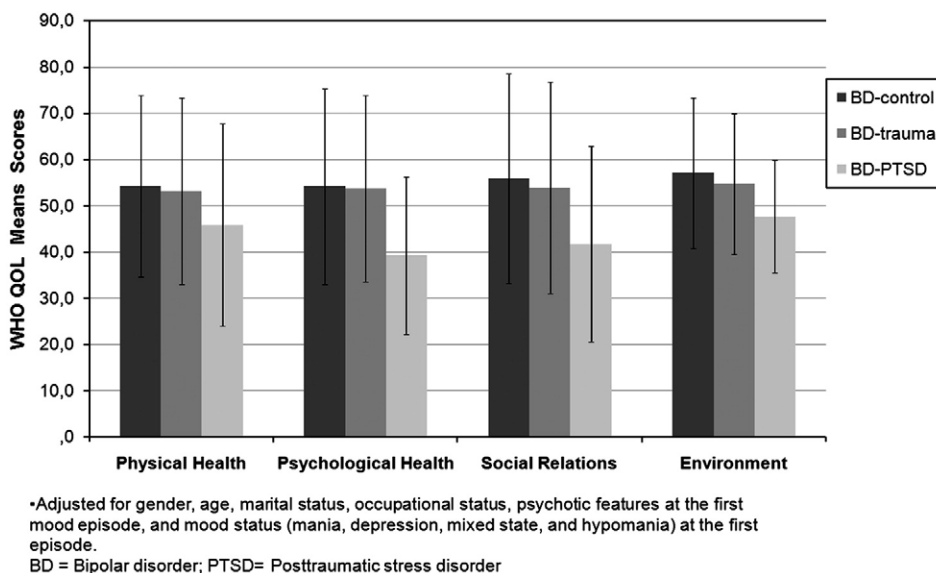


Fig. 1. Quality of life status for bipolar patients, by trauma and comorbid PTSD diagnosis.

symptoms (Gazalle et al., 2007b), female gender (Robb et al., 1998), and such subthreshold affective traits like cyclothymia (Vázquez et al., 2008) have also been suggested to play an important role in the self-perception of QOL. Additionally, even bipolar patients in remission show an impaired self-report of QOL (Sierra et al., 2005; Gazalle et al., 2007a), indicating that other factors besides mood symptoms may be involved in the determination of QOL in BD (Dias et al., 2008).

Simon et al. (2004) found that bipolar patients with PTSD had a lower likelihood of being in recovery (relative euthymia) at their study entry (Simon et al., 2004). Our results related to YMRS scores are similar, since patients with PTSD have demonstrated statistically significant differences after adjustment for covariates. Depressive symptoms were lower in the group of bipolar patients exposed to trauma but without PTSD than they were in bipolar patients with no trauma; this difference remained statistically significant after adjustment for covariates. Due to the small difference between group scores, however, this result might not have any clinical relevance. This finding was not expected but is understandable: such individuals may be resilient, since they were victims of a traumatic experience but did not develop PTSD.

Potential limitations should be addressed when drawing conclusions from this data. First, the cross-sectional design precluded the opportunity to examine chronological relationships between trauma, BD, and PTSD. Further, the study was conducted in two urban tertiary hospitals serving a low- or middle-income population; therefore, these results may not be generalized for other care service settings. Additionally, the sample size of the comorbid PTSD group was small.

5. Conclusions

Comorbid posttraumatic stress disorder appears to be an important marker of worse clinical outcomes in BD, including a higher number of suicide attempts, elevated likelihood of rapid cycling, and reduced recovery as evidenced by higher manic symptom scores. Additionally, the presence of PTSD in bipolar patients imposed a lower quality of life status relative to bipolar individuals without PTSD. Thus, PTSD comorbidity must be investigated vigorously in bipolar subjects and should be noted as an increased predictor of suicide risk. The treatments that are more favorable in BD combined with comorbid PTSD are currently unknown. More studies are required to better understand the relationship among BD, trauma, and PTSD.

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Conflict of interest

The following authors do not have any actual or potential conflict of interest, including any financial, personal, or other relationships with other people or organizations, within three years of beginning the work submitted that could inappropriately influence, or be perceived to influence, their work.

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References

- Baldassano, C.F., Marangell, L.B., Gyulai, L., Nassir Ghaemi, S., Joffe, H., Kim, D.R., Sagduyu, K., Truman, C.J., Wisniewski, S.R., Sachs, G.S., Cohen, L.S., 2005. Gender differences in bipolar disorder: retrospective data from the first 500 STEP-BD participants. *Bipolar Disord.* 7, 465–470.
- Brown, G.R., McBride, L., Bauer, M.S., Williford, W.O., 2005. Cooperative Studies Program 430 Study Team, 2005. Impact of childhood abuse on the course of bipolar disorder: a replication study in U.S. veterans. *J. Affect. Disord.* 89, 57–67.
- Carballo, J.J., Harkavy-Friedman, J., Burke, A.K., Sher, L., Baca-Garcia, E., Sullivan, G.M., Grunebaum, M.F., Parsey, R.V., Mann, J.J., Oquendo, M.A., 2008. Family history of suicidal behavior and early traumatic experiences: additive effect on suicidality and course of bipolar illness? *J. Affect. Disord.* 109, 57–63.
- Dias, V.V., Brissos, S., Frey, B.N., Kapczinski, F., 2008. Insight, quality of life and cognitive functioning in euthymic patients with bipolar disorder. *J. Affect. Disord.* 110, 75–83.
- First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B., 1997. Structured Clinical Interview for DSM-IV Axis I Disorders: Clinical Version (SCID-CV). American Psychiatric Press, Washington, DC.
- Gazalle, F.K., Frey, B.N., Hallal, P.C., Andreazza, A.C., Cunha, A.B., Santin, A., Kapczinski, F., 2007a. Mismatch between self-reported quality of life and functional assessment in acute mania: a matter of unawareness of illness? *J. Affect. Disord.* 103, 247–252.
- Gazalle, F.K., Hallal, P.C., Andreazza, A.C., Frey, B.N., Kauer-Sant'Anna, M., Weyne, F., da Costa, S.C., Santin, A., Kapczinski, F., 2007b. Manic symptoms and quality of life in bipolar disorder. *Psychiatry Res.* 153, 33–38.
- Goldberg, J.F., Garno, J.L., 2005. Development of posttraumatic stress disorder in adult bipolar patients with histories of severe childhood abuse. *J. Psychiatr. Res.* 39, 595–601.
- Gutiérrez-Rojas, L., Gurpegui, M., Ayuso-Mateos, J.L., Gutiérrez-Ariza, J.A., Ruiz-Veguilla, M., Jurado, D., 2008. Quality of life in bipolar disorder patients: a comparison with a general population sample. *Bipolar Disord.* 10, 625–634.
- Hamilton, M., 1960. A rating scale for depression. *J. Neurol. Neurosurg. Psychiatry* 23, 56–72.
- Kennedy, B.L., Dhaliwal, N., Pedley, L., Sahner, C., Greenberg, R., Manshadi, M.S., 2002. Post-traumatic stress disorder in subjects with schizophrenia and bipolar disorder. *J. Ky. Med. Assoc.* 100, 395–399.
- Kessler, R.C., Sonnega, A., Bromet, E., Hughes, M., Nelson, C.B., 1995. Posttraumatic stress disorder in the National Comorbidity Survey. *Arch. Gen. Psychiatry* 52, 1048–1060.
- Kessler, R.C., Demler, O., Frank, R.G., Olfson, M., Pincus, H.A., Walters, E.E., Wang, P., Wells, K.B., Zaslavsky, A.M., 2005. Prevalence and treatment of mental disorders, 1990 to 2003. *N. Engl. J. Med.* 352, 2515–2523.
- Merikangas, K.R., Akiskal, H.S., Angst, J., Greenberg, P.E., Hirschfeld, R.M., Petukhova, M., Kessler, R.C., 2007. Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. *Arch. Gen. Psychiatry* 64, 543–552.
- Neria, Y., Bromet, E.J., Sievers, S., Lavelle, J., Fochtmann, L.J., 2002. Trauma exposure and posttraumatic stress disorder in psychosis: findings from a first-admission cohort. *J. Consult. Clin. Psychol.* 70, 246–251.
- Neria, Y., Olfson, M., Gameroff, M.J., Wickramaratne, P., Pilowsky, D., Verdelli, H., Gross, R., Manetti-Cusa, J., Marshall, R.D., Lantigua, R., Shea, S., Weissman, M.M., 2008. Trauma exposure and posttraumatic stress disorder among primary care patients with bipolar spectrum disorder. *Bipolar Disord.* 10, 503–510.
- Otto, M.W., Perlman, C.A., Wernicke, R., Reese, H.E., Bauer, M.S., Pollack, M.H., 2004. Posttraumatic stress disorder in patients with bipolar disorder: a review of prevalence, correlates, and treatment strategies. *Bipolar Disord.* 6, 470–479.
- Robb, J.C., Young, L.T., Cooke, R.G., Joffe, R.T., 1998. Gender differences in patients with bipolar disorder influence outcome in the medical outcomes survey (SF-20) subscale scores. *J. Affect. Disord.* 49, 189–193.

- Romero, S., Birmaher, B., Axelson, D., Goldstein, T., Goldstein, B.I., Gill, M.K., Iosif, A.M., Strober, M.A., Hunt, J., Esposito-Smythers, C., Ryan, N.D., Leonard, H., Keller, M., 2009. Prevalence and correlates of physical and sexual abuse in children and adolescents with bipolar disorder. *J. Affect. Disord.* 112, 144–150.
- Sierra, P., Livianos, L., Rojo, L., 2005. Quality of life for patients with bipolar disorder: relationship with clinical and demographic variables. *Bipolar Disord.* 7, 159–165.
- Simon, N.M., Otto, M.W., Wisniewski, S.R., Fossey, M., Sagduyu, K., Frank, E., Sachs, G.S., Nierenberg, A.A., Thase, M.E., Pollack, M.H., 2004. Anxiety disorder comorbidity in bipolar disorder patients: data from the first 500 participants in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). *Am. J. Psychiatry* 161, 2222–2229.
- Simon, N.M., Pollack, M.H., Ostacher, M.J., Zalta, A.K., Chow, C.W., Fischmann, D., Demopulos, C.M., Nierenberg, A.A., Otto, M.W., 2007. Understanding the link between anxiety symptoms and suicidal ideation and behaviors in outpatients with bipolar disorder. *J. Affect. Disord.* 97, 91–99.
- Vázquez, G.H., Kahn, C., Schiavo, C.E., Goldchluk, A., Herbst, L., Piccione, M., Saidman, N., Ruggeri, H., Silva, A., Leal, J., Bonetto, G.G., Zaratiegui, R., Padiilla, E., Vilapriño, J.J., Calvo, M., Guerrero, G., Strejilevich, S.A., Cetkovich-Bakmas, M.G., Akiskal, K.K., Akiskal, H.S., 2008. Bipolar disorders and affective temperaments: a national family study testing the “endophenotype” and “subaffective” theses using the TEMPS-A Buenos Aires. *J. Affect. Disord.* 108, 25–32.
- WHOQOL Group, 1998. Development of the World Health Organization WHOQOL-BREF quality of life assessment. *Psychol. Med.* 28, 551–558.
- Young, R., Biggs, J., Ziegler, V., Meyer, D., 1978. A rating scale for mania: reliability, validity and sensitivity. *Br. J. Psychiatry* 133, 429–435.