

Brief Report

Post-traumatic stress disorder among adolescents with bipolar disorder and its relationship to suicidality

Dilsaver SC, Benazzi F, Akiskal HS, Akiskal KK. Post-traumatic stress disorder among adolescents with bipolar disorder and its relationship to suicidality.

Bipolar Disord 2007; 9: 649–655. © Blackwell Munksgaard, 2007

Objectives: The aims of this cross-sectional pilot study were to ascertain the rates of post-traumatic stress disorder (PTSD) among adolescents with bipolar disorder (BPD) and major depressive disorder (MDD) relative to a comparison group comprised of non-affectively ill patients, and to determine whether PTSD is related to suicidal ideation and attempts. The impetus for the study was born of clinical impressions derived in the course of routine clinical practice.

Methods: Patients were screened by a single interviewer for BPD, MDD and PTSD, panic disorder, obsessive-compulsive disorder (OCD) and social phobia using the apposite modules from the Structured Clinical Interview for DSM-IV (SCID) and histories of suicidal ideation and attempts. The data were subjected to analysis using a logistic regression model.

Results: The database included 34 patients with BPD, 79 with MDD and 26 with a non-affective disorder. The risk for PTSD for a patient with BPD significantly exceeded that for a patient with MDD [odds ratio (OR) = 4.9, 95% confidence interval (CI) = 1.9–12.2, $p = 0.001$]. Patients with PTSD had an insignificantly increased risk for suicidal ideation (OR = 2.8, 95% CI = 0.9–8.9, $p = 0.069$), and a 4.5-fold significantly increased risk of having had a suicide attempt (OR = 4.5, 95% CI = 1.7–11.7, $p = 0.002$). The relationship between PTSD and suicide attempts remained significant even after controlling for the confounding effects of concurrent panic disorder, OCD and social phobia (OR = 3.4, 95% CI = 1.1–10.0, $p = 0.023$).

Conclusions: Patients with BPD have a greater risk for PTSD than those with MDD. Post-traumatic stress disorder is significantly related to history of suicide attempts.

Steven C Dilsaver^{a,b}, Franco Benazzi^c, Hagop S Akiskal^{d,e,f} and Karen K Akiskal^g

^aMental Health Mental Retardation Clinic, Rio Grande City, TX, ^bHaraszti and Associates, Pasadena, CA, USA, ^cDepartment of Psychiatry, National Health Service, Forli, Italy, ^dDepartment of Psychiatry, ^eInternational Mood Center, University of California at San Diego, San Diego, ^fVeterans Administration Medical Center, La Jolla, CA, USA, ^gNational Union of Depressive and Manic-depressive Association, Rennes, France

Key words: affective disorders – anxiety disorders – bipolar disorder – post-traumatic stress disorder – suicide

Received 5 July 2005, revised and accepted for publication 5 May 2006

Corresponding author: Steven C Dilsaver, MD, 4953 Hellman Avenue, Los Angeles, CA 90042, USA. Fax: +1 323-344-8711; e-mail: stevendilsaver@aol.com

It is now well accepted that unipolar major depressive disorder (MDD) is often complicated by the simultaneous presence of anxiety disorders. Data also indicate that the presence of various

forms of comorbidity is the rule rather than the exception among adults with bipolar disorder (BPD) (1, 2). For more than a decade, a strong relationship between panic and BPD has been consistently demonstrated in epidemiological (3) and clinical (4–8) samples. A similar relationship between bipolarity and obsessive-compulsive disorder (OCD) has also been reported (8–12). In sum, panic disorder, OCD and social phobia are all

The authors of this paper do not have any commercial associations that might pose a conflict of interest in connection with this manuscript.

common sources of suffering and disability among bipolar adults (1–17).

Unfortunately, our knowledge base on the topic of anxiety disorder comorbidity among youth with BPD remains meager. Recently, investigators concluded that the diagnosis of BPD in youth is in and of itself a significant risk factor for comorbid anxiety disorders (18). However, the database used by these investigations did not provide for the comparison of subjects with BPD and MDD. In a recently completed study (19), we have addressed this issue by showing that adolescents with BPD are at particularly high risks for panic disorder, OCD and social phobia *relative to those with MDD*. We found that comorbidity for these disorders is cumulative (these anxiety disorders are risk factors for one another) and that increasing anxiety disorder burden increased the odds of suicidal ideation, suicide attempts and other correlates of severity of illness (19).

Other emerging literature indicates that anxious bipolarity increases the global severity of illness and poor outcome to existing somatic treatments (20–28). However, post-traumatic stress disorder (PTSD) has been typically excluded from this literature.

Impressions derived exclusively in the course of ordinary, routine, mundane clinical practice led us to conduct the present cross-sectional study. These impressions led us to hypothesize that the rate of comorbidity for PTSD is greater among bipolar than unipolar adolescents, and that PTSD is related to the presence of suicidal ideation and attempts even after accounting for the potentially confounding effects of panic disorder, OCD and social phobia. The results of a cross-sectional study addressing this topic are presented in this article.

Methods

Clinical setting

We evaluated, in and through the process of delivering ordinary, routine clinical services, a consecutive series of adolescent patients between 12 and 17 years of age, who presented in a public sector outpatient clinic for the destitute in a rural county in southern Texas, a notoriously impoverished region of the USA. The county had a population of approximately 53,000 persons in the 2000 census.

The racial composition of the county is 99% Latino and 1% other. This is highly relevant. Latino families in the community in which the clinic was situated dedicate all the resources at their

disposal, through sacrifices exerted by nuclear and extended family, to avoiding hospitalization. Many patients in this database would have been hospitalized in other cultural settings. Further, hospitalization was not an available option for our patients except under the most extreme of circumstances. Hospital resources for adolescents required transport to a state facility four hours removed from home. Allowing such an event to take place is alien to the traditional cultural beliefs of the population under study.

The county in which this work was carried out constitutes a closed rural community; there is for all intents and purposes no movement into it. This scenario for inbreeding tends to support our perception that there is a high rate of bipolarity among the citizenry of the county. Others working in closed communities have reported the same perception. Perhaps the best example of this potential effect of inbreeding is provided by the Old Order Amish population of Pennsylvania (29, 30).

The clinic from which we sourced the data yielding the findings presented herein is the only vehicle for the delivery for psychiatric services in the county. The first author (SCD) was the only permanent psychiatrist in the 150-year history of the county and was the sole practitioner of psychiatry in the entire region.

All patients seen at the clinic underwent the same psychiatric assessment, as did the adolescents who provided the data that made this cross-sectional study possible. The thorough patient evaluations carried out constituted standard practice in the clinic and were not parcel to the dictates of a research protocol. In this setting, oral informed consent to the evaluative process and the recording of clinical findings were routinely carried out to meet the fundamental needs of patients.

Interview procedures and diagnostic groups

All patients were medication-naïve at the time of assessment. Each patient underwent a structured screening for the occurrence of a major depressive episode (MDE) with concurrent hypomania or mania, panic disorder, OCD, social anxiety disorder and PTSD using the modules for these disorders as extracted from Structured Clinical Interview for DSM-IV Clinician Version (SCID-CV) (31). The anxiety disorders reported pertained to psychopathology present at the time of interview. A patient with delusions or hallucinations was classified as having psychotic features. None of the subjects had formal thought disorder.

Family history of MDD or BPD among first-degree relatives was obtained either by live interview or interview by proxy. Interview by proxy necessitated that at least one family member be interviewed using the modules for MDE and hypomania/mania included in the SCID-CV. In this small, family-oriented community, access to first-degree relatives came with remarkable ease. However, not all first-degree relatives were available for live interview. Consequently, it was necessary to interview slightly under 50% of them by proxy. Rendering a diagnosis by proxy demanded the strict criterion that the relative in question unequivocally met the full criteria for MDD or BPD. This method of ascertaining the presence of affective illness in first-degree relatives was a normative practice in the clinic regardless of a patient's presenting complaint or the reason for referral.

Patients were placed in one of three categories: (i) Those who met DSM-IV (32) criteria for BPD depressed, BPD II depressed or mixed states. Patients with pure mania who had never had a MDE were excluded, as pure mania appears to strongly inhibit panic (7, 33, 34). (ii) Those who met criteria for MDE who had never had a hypomanic or manic episode. These patients were classified as having MDD. (iii) Psychiatric patients who did not meet the criteria for BPD or MDD constituted a comparison control group (CG). This third group of patients included, but was not limited to, patients with primary diagnoses of adjustment disorder, alcohol or substance abuse disorders, oppositional defiant disorder, conduct disorder or no Axis I disorder. Patients with substance abuse disorders and conduct disorder are often quite anxious. However, these individuals were not excluded. (In contrast, patients with primary diagnoses of non-affective *psychotic* disorders were excluded as they may have had illnesses that placed them at high risk for anxiety disorder comorbidity and thereby warranted attention in a parallel study.)

A suicide attempt was operationally defined as any physically self-destructive act cognitively associated with preoccupation with the termination of life. This act did not need to be serious from a medical perspective. This definition has proven useful in previously published work (35).

Most cases of PTSD in our series were associated with sexual abuse. In the other instances the precipitating trauma stemmed from being the victim of or witnessing a violent crime. The occurrence of the trauma was determined by the direct report of the victim (patient). We did not have access to court records or any other archival

material that would have allowed otherwise. The overall clinical assessments led us to conclude that the traumatic events resulting in PTSD preceded the overt onset of the mood disorder.

By its very nature, trauma makes it difficult for victims to articulate its onset and various parameters in a precise manner. Such data should ideally be collected on a prospective basis, and should rely on records. However, in clinical work this material is often obtained retrospectively and qualitatively.

Statistics

Measures of variance in mean values refer to the standard deviation of the mean (SD). A logistic regression model was used to determine whether patients with BPD were more likely to have PTSD than those with MDD and those with MDD more likely than CG patients. The confounding effects of simultaneous comorbid panic disorder, OCD and social phobia were controlled for using this model. A logistic regression model was also used to determine whether the presence of PTSD conferred increased risk for a history of suicidal ideation and suicide attempts. Statistical analyses were performed using STATA Version 8.2 (STATA Corp., College Station, TX, USA). The level of significance was set for $p < 0.05$, two-tailed.

Results

Thirty-four patients had BPD, 79 MDD and 26 a non-affective disorder. The characteristics of the study sample are summarized in Table 1.

The risk for PTSD of BPD patients exceeded that of MDD patients 4.9-fold [odds ratio (OR) = 4.9, 95% confidence interval (CI) = 1.9–12.2, $p = 0.001$]. The risk for PTSD of MDD patients did

Table 1. Characteristics of study sample

Variables, mean %	BPD (n = 34)	MDD (n = 79)	CG (n = 26)
Age, years (SD)	14.8 (1.6)	14.6 (1.6)	14.4 (1.1)
Females	55.8	65.8	42.3
PTSD	38.2	13.9	3.8
Panic disorder	41.1	16.4	3.8
OCD	47.0	13.9	0.0
Social phobia	38.2	15.1	3.8
Suicidal ideation	88.2	73.4	26.9
Suicide attempt	52.9	49.3	11.5
BPD-FH	32.3	15.1	0.0
MDD-FH or BPD-FH	64.6	40.4	7.6

BPD = bipolar disorder; MDD = major depressive disorder; CG = comparison group; PTSD = post-traumatic stress disorder; OCD = obsessive-compulsive disorder; BPD-FH = bipolar disorders family history in first-degree relatives; MDD-FH = major depressive disorder family history in first-degree relatives.

not exceed that of the comparison patients (OR = 0.5, 95% CI = 0.2–1.3, $p = 0.185$).

Patients with PTSD had a 2.8-fold increase in the risk of having suicidal ideation; however, this failed to reach significance (OR = 2.8, 95% CI = 0.9–8.9, $p = 0.069$). Patients with PTSD had a 4.5-fold increase in the risk of having had a suicide attempt (OR = 4.5, 95% CI = 1.7–11.7, $p = 0.002$). Post-traumatic stress disorder was associated with a 4.2-fold increase in the risk of having had a suicide attempt after controlling for the presence of BPD (OR = 4.2, 95% CI = 1.5–11.4, $p = 0.004$).

The relationship between PTSD and suicide attempts remained significant after controlling for the confounding effects of each of the other three anxiety disorders. The risk of having had a suicide attempt was 3.7-fold greater among the patients with PTSD after controlling for the confounding effect of panic disorder (OR = 3.7, 95% CI = 1.3–10.3, $p = 0.009$), 3.9-fold greater after controlling for the effect of OCD (OR = 3.9, 95% CI = 1.4–11.1, $p = 0.009$) and 4.1-fold greater after controlling for the effect of social phobia (OR = 4.1, 95% CI = 1.4–11.4, $p = 0.006$). The relationship between PTSD and suicide attempts remained significant after controlling for all possible combinations of panic disorder, OCD and social phobia (OR = 3.4, 95% CI = 1.1–10.1, $p = 0.023$).

Discussion

Methodological issues

We will first address the limitations of our study dictated by the clinical setting. We restricted this study to panic disorder, OCD and social phobia and PTSD out of pure necessity. Other disorders such as generalized anxiety disorder would ideally have been included in the statistical models. However, SCD worked under major time constraints, routinely seeing and conducting diagnostic interviews with 20 patients over the course of a long day. He was forced to streamline the evaluation process to include only the disorders that appeared to be the most common, impairing and clinically relevant. Initially panic disorder, OCD and social anxiety disorder appeared to be the only anxiety disorders to meet these criteria. As shown elsewhere (19), statistical modeling indicates that the aggregate number of these three disorders relates to correlates of the severity of illness, such as the presence of psychosis, suicidal ideation, suicide attempts, and alcohol and drug abuse.

It was not until long into his course of service to the people of this county that SCD learned that

PTSD is a very common disorder among bipolar adolescents. He then embarked on the process of routinely conducting structured screening for the presence of this disorder. This accounts for the relatively modest number of patients in the database used in the preparation of this particular report. Admittedly, the sample size and post hoc addition of PTSD constitute limitations of this inquiry.

Another potential limitation is that time constraints required that we use an evaluative procedure that could be applied to both adolescents and adults. The SCID is not generally used in the assessment of adolescents. Ideally, an interview schedule modified to include screening for the anxiety disorders in question and designed for the evaluation of children and adolescents, such as the Diagnostic Interview for Children and Adolescents (DICA), would have been utilized (36). However, regardless of the interview schedule utilized, a patient would have had to meet the full DSM-IV criteria for BPD, MDD and each of the anxiety disorders in question to justify these diagnoses. That is, regardless of the interview schedule employed, a patient would have to fulfill the criteria for a disorder as specified in the SCID. Perfect correspondence between criteria for the operational definitions of BPD, MDD, panic disorder, OCD, social phobia and PTSD is essential to the validity of this study, and the SCID fulfills this requirement. Thus, the results of this process of ascertaining the presence of the disorders under study are fully congruent with those that would have been attained if another interview format had been employed.

Studying a Latino population raises concerns about the generalizability of our findings. However, focus on this population actually lends strength to the study. The Latino population of Mexican origin is the most rapidly growing segment of the populace in the USA. Yet the clinical literature on mood disorders among Latino youth is limited to reports by us (e.g., see 19, 35, 37–41). Research on the topic of psychopathology among Latino youth is of major public health importance and deserves the attention of other investigators.

Bipolarity, PTSD and suicidality

To the best of our knowledge, the present paper is the first to compare PTSD in juvenile BPD and MDD patients. Otto et al. (42) reviewed the literature on the topic of comorbid PTSD among bipolar *adults*. This review indicated that the mean prevalence of PTSD in bipolar patients is 16.0%, a

rate that is about twice the lifetime prevalence of PTSD in the general population. However, their review did not include literature on juvenile onset PTSD in bipolar patients, information about the relative frequencies of comorbid PTSD in bipolar and unipolar probands, or data on the rates of suicidal ideation and attempts in PTSD. This article is, to the best of our knowledge, the first pertaining to these topics.

Bipolar disorder is associated with a lifetime rate of suicide attempts in adults of 25–50% (43, 44). In our juvenile sample, we found that the presence of PTSD was associated with an increased risk of suicide attempts after controlling for the mere presence of BPD. This is a very important finding. It indicates that PTSD mediates risk for suicide attempts independently of comorbid BPD. Post-traumatic stress disorder also remained significantly related to suicide attempts after controlling for the presence of panic disorder, OCD and social phobia and all combinations of these comorbid anxiety disorders. Thus, the relationship between PTSD and suicide attempts is not an artifact of the confounding effect of these common comorbid anxiety disorders in subjects with BPD. The results suggest that PTSD might represent an independent risk factor for suicide attempts. This might be in part mediated by the futurelessness/hopelessness cognitions of PTSD; such cognitions are well known correlates of suicidality (45).

Sexual trauma, PTSD and bipolarity

We found only one *adult* study among veterans reporting sexual trauma, PTSD and bipolarity (46). However, that study did not make comparisons with MDD patients and left the direction of causality uncertain. The high rate of comorbidity between PTSD and BPD in our juvenile patients raises many important questions about the role of trauma in the link between PTSD and bipolarity. Our data suggest that the trauma leading to PTSD most likely occurred early in life and preceded the overt onset of the BPD. However, it is known that BPD has an insidious onset with subthreshold symptoms that can long predate its overt manifestations (47, 48).

It is not improbable that both internalizing and externalizing signs and symptoms that precede overt BPD (48) may make a child vulnerable to being abused. For example, an anxious child who is 'passive' may be seen as inviting prey to abusive individuals. By contrast, behaviors related to extraversion and hypersexuality (49) – which occur even among preschoolers (50) – may give false cues to sexually predatory adults. It is also

likely that the emotional state of some children who are in the process of developing overt BPD clouds their judgment in relation to adults who approach them sexually. Finally, one must consider the possible deleterious impact of a chaotic emotional climate in a family with bipolar adults (51, 52). In summary, we propose a model in which PTSD and BPD and/or their precursors interact in a complex manner. Only prospective studies can unravel the definitive pathways involved in this relationship.

References

1. Kessler RC, Chiu WT, Demier O, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Replication. *Arch Gen Psychiatry* 2005; 62: 617–627.
2. McElroy SL, Altshuler LL, Suppes T et al. Axis I psychiatric comorbidity and its relationship to historical illness variables in 288 patients with bipolar disorder. *Am J Psychiatry* 2001; 158: 420–426.
3. Chen YW, Dilsaver SC. Comorbidity of panic disorder in bipolar illness: evidence from the Epidemiologic Catchment Area Survey. *Am J Psychiatry* 1995; 152: 280–282.
4. Savino M, Perugi G, Simonini E, Soriani A, Cassano GB, Akiskal HS. Affective comorbidity in panic disorder: is there a bipolar connection? *J Affect Disord* 1993; 28: 155–163.
5. MacKinnon DF, Zandi PP, Gershon ES, Nurnberger JI, DePaulo JR. Association of rapid mood switching with panic disorder and familial panic risk in familial bipolar disorder. *Am J Psychiatry* 2003; 160: 1696–1698.
6. MacKinnon DF, Zandi PP, Cooper J et al. Comorbid bipolar disorder and panic disorder in families with a high prevalence of bipolar disorder. *Am J Psychiatry* 2002; 159: 30–35.
7. Dilsaver SC, Chen YW. Social phobia, panic disorder and suicidality in subjects with pure and depressive mania. *J Affect Disord* 2003; 77: 173–177.
8. Perugi G, Akiskal HS, Toni C, Simonini E, Gemignani A. The temporal relationship between anxiety disorders and (hypo)mania: a retrospective examination of 63 panic, social phobic and obsessive-compulsive patients with comorbid bipolar disorder. *J Affect Disord* 2001; 67: 199–206.
9. Chen YW, Dilsaver SC. Comorbidity for obsessive-compulsive disorder in bipolar and unipolar disorders. *Psychiatry Res* 1995; 59: 57–64.
10. Perugi G, Toni C, Frare F, Traverso MC, Hantouche E, Akiskal HS. Obsessive-compulsive–bipolar comorbidity: a systematic exploration of clinical features and treatment outcome. *J Clin Psychiatry* 2003; 63: 1129–1134.
11. Hantouche EG, Angst J, Demonfaucon C, Perugi G, Lancrenon S, Akiskal HS. Cyclothymic OCD: a distinct form? *J Affect Disord* 2003; 75: 1–10.
12. Angst J, Gamma A, Endrass J et al. Obsessive-compulsive syndromes and disorders: significance of comorbidity with bipolar and anxiety syndromes. *Eur Arch Clin Neurosci* 2005; 255: 65–71.
13. Gordon A, Rasmussen SA. Mood-related obsessive-compulsive symptoms in a patient with bipolar affective disorder. *J Clin Psychiatry* 1988; 49: 27–28.

14. Kruger S, Cooke RG, Hasey GM, Jorna T, Persad E. Comorbidity of obsessive compulsive disorder in bipolar disorder. *J Affect Disord* 1995; 34: 117–120.
15. Kruger S, Braunig P, Cooke RG. Comorbidity of obsessive-compulsive disorder in recovered inpatients with bipolar disorder. *Bipolar Disord* 2000; 2: 71–74.
16. Perugi G, Akiskal HS, Pfanner C et al. The clinical impact of bipolar and unipolar affective comorbidity on obsessive-compulsive disorder. *J Affect Disord* 1997; 46: 15–23.
17. Boylan KR, Bieling PJ, Marriott M, Begin H, Young LT, MacQueen G. Impact of comorbid anxiety disorders on outcome in a cohort of patients with bipolar disorder. *J Clin Psychiatry* 2004; 65: 1106–1113.
18. Harpold TL, Wozniak J, Kwon A et al. Examining the relationship between pediatric bipolar disorder and anxiety disorders in psychiatrically referred children and adolescents. *J Affect Disord* 2005; 88: 19–26.
19. Dilsaver SC, Akiskal HS, Akiskal KK, Benazzi F. Dose-response relationship between number of comorbid anxiety disorders in adolescent bipolar/unipolar disorders, and psychosis, suicidality, substance abuse and familiarity. *J Affect Disord* 2006; 96: 249–258.
20. Feske U, Frank E, Mallinger AG et al. Anxiety as a correlated of response to the acute treatment of bipolar disorder. *Am J Psychiatry* 2000; 157: 956–962.
21. Freeman MP, Freeman SA, McElroy SL. The comorbidity of bipolar and anxiety disorders: prevalence, psychobiology and treatment issues. *J Affect Disord* 2002; 68: 1–23.
22. Goodwin RD, Hoven CW. Bipolar-panic comorbidity in the general population: prevalence and associated morbidity. *J Affect Disord* 2003; 70: 27–33.
23. Simon NM, Otto MW, Weiss RD et al. Pharmacotherapy for bipolar disorder and comorbid conditions: baseline data from STEP-BD. *J Clin Psychopharmacol* 2004; 24: 512–520.
24. Selma F, Bellivier F, Henry C et al. Bipolar patients with suicidal behavior: toward the identification of a clinical subgroup. *J Clin Psychiatry* 2004; 65: 1035–1039.
25. Cassano GB, Pini S, Sacttoni M, Dell’Osso L. Multiple anxiety disorder comorbidity in patients with mood spectrum disorders with psychotic features. *Am J Psychiatry* 1999; 156: 474–476.
26. Frank E, Cyranowski JM, Rucci P et al. Clinical significance of lifetime panic spectrum symptoms in the treatment of bipolar I disorder. *Arch Gen Psychiatry* 2002; 59: 905–911.
27. Henry C, Van den Bulke D, Bellivier F, Etain B, Rouillon F, Leboyer M. Anxiety disorders in 318 bipolar patients: prevalence and impact on illness severity and response to mood stabilizer. *J Clin Psychiatry* 2003; 64: 331–335.
28. Simon NM, Otto MW, Wisniewski SR et al. 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* 2004; 161: 2222–2229.
29. Egeland JA. A genetic study of manic-depressive disorder among old order Amish of Pennsylvania. *Pharmacopsychiatry* 1988; 21: 74–75.
30. Egeland JA. Description of the Amish dataset. *Genet Epidemiol* 1989; 6: 195–199.
31. First MB, Gibbon M, Spitzer RC, Williams JBW, Benjamin LS. Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version (SCID-CV). Washington DC: American Psychiatric Association Press, 1997.
32. APA Task Force on Nomenclature. *Diagnostic and Statistical Manual of Mental Disorders*, 4th edn. Washington DC: APA Press, 1994.
33. Shoaib AM, Dilsaver SC. Panic disorder in pure and depressive mania. *Anxiety* 1994; 1: 302–304.
34. Dilsaver SC, Chen YW, Swann AC, Shoaib AM, Tsai-Dilsaver Y, Krajewski KJ. Suicidality, panic disorder and psychosis in bipolar depression, depressive-mania and pure-mania. *Psychiatry Res* 1997; 73: 47–56.
35. Dilsaver SC, Benazzi F, Rihmer Z, Akiskal KK, Akiskal HS. Gender, suicidality and mixed states. *J Affect Disord* 2005; 87: 11–16.
36. Reich W. Diagnostic interview for children and adolescents (DICA). *J Am Acad Child Adolesc Psychiatry* 2000; 39: 59–66.
37. Dilsaver SC, Akiskal HS. Preschool mania in Hispanic children: incidence, phenomenology and family history. *J Affect Disord* 2004; 82 (Suppl.): 35–43.
38. Dilsaver SC, Akiskal HS. High rate of bipolar mixed states among destitute Hispanic adolescents referred for ‘major depressive disorder’. *J Affect Disord* 2005; 84: 179–186.
39. Dilsaver SC, Benazzi F, Akiskal HS. The mixed state: the most common outpatient presentation among bipolar depressed adolescents in a community mental health clinic? *Psychopathology* 2005; 38: 268–272.
40. Dilsaver SC, Cao X, Manning S, Akiskal HS. Pain complaints in adolescents: patients with affective disorders versus psychiatric controls. *Prim Care Companion J Clin Psychiatry* 2005; 7: 150–154.
41. Dilsaver SC, Henderson-Fuller S, Akiskal HS. Occult mood disorders in 104 consecutively presenting children referred for the treatment of attention-deficit/hyperactivity disorder in a community mental health clinic. *J Clin Psychiatry* 2003; 64: 170–176.
42. Otto MW, Perlman CA, Wernicke R, Reese HE, Bauer MS, Pollack MH. Post-traumatic stress disorder in patients with bipolar disorder: a review of prevalence, correlates and treatment strategies. *Bipolar Disord* 2004; 6: 470–479.
43. Chen YW, Dilsaver SC. Lifetime rates of suicide attempts among subjects with bipolar and unipolar disorders relative to subjects with other Axis I disorders. *Biol Psychiatry* 1996; 15: 896–899.
44. Jamison KR. Suicide and bipolar disorder. *J Clin Psychiatry* 2000; 61 (Suppl. 9): 47–51.
45. Beck AT, Steer RA, Kovacs M, Garrison B. Hopelessness and eventual suicide: a 10-year prospective study of patients hospitalized with suicidal ideation. *Am J Psychiatry* 1985; 142: 559–563.
46. Brown GR, McBride L, Bauer MS, Williford WO, Cooperative Studies Program 430 Study Team. Impact of childhood abuse on the course of bipolar disorder: a replication study in US veterans. *J Affect Disord* 2005; 89: 57–67.
47. Akiskal HS, Downs J, Jordan P, Watson S, Daugherty D, Pruitt DB. Affective disorders in the referred children and younger siblings of manic-depressives: mode of onset and prospective course. *Arch Gen Psychiatry* 1985; 42: 996–1003.
48. Shaw JA, Egeland JA, Endicott J, Allen CR, Hostetter AM. A 10-year prospective study of prodromal patterns for bipolar disorder among Amish youth. *J Am Acad Child Adolesc Psychiatry* 2005; 44: 1104–1117.
49. Geller B, Zimmerman B, Williams M, Delbello MP, Frazier J, Beringer L. Phenomenology of prepubertal and early adolescent bipolar disorder: examples of elated mood, grandiose behaviors, decreased need for sleep,

Post-traumatic stress disorder in bipolar disorder

- racing thoughts and hypersexuality. *J Child Adolesc Psychopharmacol* 2002; 12: 3–9.
50. Moto-Castillo M, Torruella A, Engels B, Perez J, Dedrick C, Gluckman M. Valproate in very young children: an open case series with a brief follow-up. *J Affect Disord* 2001; 67: 194–197.
51. Akiskal HS. The temperamental foundations of mood disorders. In: Mundt CH ed. *Interpersonal Factors in the Origin and Course of Affective Disorders*. London: Gaskell, 1996: 3–30.
52. Levitan RD, Parikh SV, Lesage AD et al. Major depression in individuals with a history of childhood physical or sexual abuse: relationship to neurovegetative features, mania and gender. *Am J Psychiatry* 1998; 155: 1746–1752.

Copyright of Bipolar Disorders is the property of Blackwell Publishing Limited and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.

Copyright of Bipolar Disorders is the property of Blackwell Publishing Limited and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.