ELSEVIER

Journal of Affective Disorders 73 (2003) 33–38

JOURNAL OF AFFECTIVE DISORDERS

www.elsevier.com/locate/jad

Research report

Refining the evaluation of bipolar II: beyond the strict SCID-CV guidelines for hypomania

Franco Benazzi[a,*], Hagop S. Akiskal[b]

[a]*Department of Psychiatry, National Health Service, Forli, Italy*
[b]*Department of Psychiatry, International Mood Center, VA Medical Center, University of California, San Diego, CA, USA*

Received 23 April 2001; accepted 31 October 2001

Abstract

Background: The prevalence of bipolar II disorder in depressed outpatients is much higher than previously reported, a finding probably related to systematic probing for past hypomania by trained clinicians. Our objective was to further refine the strict SCID-CV guidelines for hypomania in depressed outpatients. *Methods:* 168 consecutive outpatients presenting with major depression were systematically interviewed with the SCID-CV about all past hypomanic behavior, irrespective of duration and initial negative response to the screening question on mood. Once typical hypomanic behaviors were elicited, the patient was re-questioned about mood change. *Results:* The prevalence of bipolar II was 61.3%. Bipolar II, so-defined, was indistinguishable at age of onset, recurrence, and atypical features from a previous sample of 251 BP-II patients interviewed by the same clinician (FB) without the present modification of the stem question on mood, and which had yielded a prevalence of 45% in the same outpatient clinic. *Limitations:* Single interviewer, and cross-sectional assessment. *Conclusions:* Systematic probing for all past hypomanic symptoms and behaviors, independently of the answer to the screening question on mood, can elicit hypomanic features that would otherwise be discarded by strict adherence to the SCID-CV. A net gain of 16% in the diagnosis of BP-II can thereby be achieved.

Keywords: Major depression; Hypomania; Bipolar II disorder; Prevalence; Diagnosis; SCID-CV

1. Introduction

A bipolar spectrum community prevalence of 5–8.3% was recently reported (Angst, 1998), versus the 1.2–1.6% reported in more conventional studies such as the Epidemiologic Catchment Area (ECA) study (Regier et al., 1988) and the National Comorbidity Study (Kessler et al., 1994). Furthermore, in samples of depressed outpatients, the prevalence of bipolar II has been reported to be 30–55% (Akiskal and Mallya, 1987; Cassano et al., 1992; Benazzi, 1997a;

*Corresponding author. Via Pozzetto 17, 48015 Castiglione di Cervia RA, Italy. Tel.: +39-335-619-1852; fax: +39-0543-30069.

E-mail address: f.benazzi@fo.nettuno.it (F. Benazzi).

0165-0327/02/$ – see front matter
PII: S0165-0327(02)00327-0

Hantouche et al., 1998). In a primary care psychiatric setting, bipolar spectrum disorders were found to be 60%, and many 'unipolar' depressives were deemed bipolar when patient assessment was made by trained clinicians systematically interviewing about past hypomania (Ghaemi et al., 2000). Even in a nonpsychiatric general medical setting, the prevalence of bipolar II has been observed in one of three patients presenting with depression or anxiety (Manning et al., 1997). The apparent increased prevalence of bipolar II may be related to systematic questioning of depressed patients about past hypomania (Dunner and Tay, 1993; Benazzi, 1997a; Hantouche et al., 1998; Akiskal et al., 2000). There is converging evidence that the minimum duration of hypomania for bipolar II diagnosis is less than the 4 days required by DSM-IV [a cut-off not based on data (Akiskal et al., 1977, 1979, 2000; Coryell et al., 1995; Akiskal, 1996; Angst, 1998; Dunner, 1998)]. The high prevalence of bipolar II defined more broadly than in DSM-IV in both community and clinical settings is contrary to Baldessarini's (2000) plea to limit the boundaries of bipolar disorder.

Skillful systematic questioning about past hypomania, supplemented by collateral information from family members and close friends, is required to make the diagnosis of bipolar II (Akiskal et al., 2000). The diagnosis of bipolar II now has a low reliability because it is based on patient's and informants' memory (state dependent) and on the interviewer's skills (Akiskal and Pinto, 1999). The reliability of bipolar II diagnosis may also be compromised by lack of clear boundaries between mania and hypomania in DSM-IV (Coryell, 1999; Akiskal et al., 2000). The inter-rater reliability of bipolar II diagnosis is high with clinical interviews, and low with structured interviews (Rice et al., 1986; Dunner, 1996; Coryell, 1999). Poor reliability between diagnoses made by nonclinicians using structured interviews and by clinicians using nonstructured–semistructured interviews has been reported (Steiner et al., 1995; Brugha et al., 1999a). Structured interviews may reduce the validity, since there is no clinical evaluation (Brugha et al., 1999b). Dunner and Tay (1993) found that trained clinicians using a semistructured interview, versus nonclinicians using a structured interview, made a diagnosis of bipolar II more often, and had a high degree of diagnostic agreement. These authors also reported that the screening question on mood was a major limitation of the DSM-III structured interview for hypomania, as it limited the systematic assessment of all hypomanic symptoms. These considerations suggest that Baldessarini's (2000) plea is unnecessarily cautious. As documented in the foregoing discussion, methodologies do exist for the skillful elicitation of key features of bipolar II. In the present study we further sought to improve upon the foregoing methodologies.

The Structured Clinical Interview for DSM-IV Axis I Disorders—Clinician Version (SCID-CV, First et al., 1997) is a partly semistructured interview for use by clinicians. It has structured questions, but ratings are based on clinical evaluation, and clinicians can ask additional questions to make the meaning of the question clearer. However, in the assessment of hypomanic episodes, if the mood screening question is negative, clinicians are expected to skip-out the assessment of all other hypomanic symptoms. To improve the assessment of past hypomania, in the present study the SCID-CV skip-out instruction of the screening question on hypomanic mood was not followed, and all hypomanic symptoms and behaviors were assessed. Also, in accordance with the current international consensus (see Akiskal et al., 2000) and the interviewing experience of the clinician (FB) in the 'Ravenna studies' (Benazzi and Rihmer, 2000), a modal duration of hypomania of 2 days rather than the DSM-IV cut-off of 4 days was followed. The aim of the study was to determine the prevalence of bipolar II in depressed outpatients using the modified SCID-CV.

2. Methods

The data reported here were derived from the psychiatry outpatient private practice of the first author (FB). Private practice was chosen because it is more representative of mood disorder patients spontaneously seeking psychiatric treatment in Italy, where it is the first (or the second, after family medicine) setting for treatment of mood disorders, in contrast to the most severe mood patients who are usually treated in national psychiatric health services

or in university centers. Actually, mood disorder patients in academic centers may not be representative of typical mood disorder patients (Goldberg and Kocsis, 1999; Akiskal and Pinto, 1999). 168 consecutive patients, presenting spontaneously for major depressive episode (MDE) treatment, were interviewed over a period of 13 months. Substance abuse and severe personality disorder patients (diagnosed by clinical interview using DSM-IV criteria) were not included, because they may confound the diagnosis of bipolar II (Akiskal et al., 2000). Actually, in the present study setting, the prevalence of bipolar II and unipolar patients with severe personality disorder was found to be relatively low (Benazzi, 2000). Those with disabling medical conditions were also excluded. Patients were interviewed by FB during the first visit (cross-sectional assessment) using the SCID-CV (First et al., 1997) mood disorder module: all patients were interviewed using SCID-CV for history of manic/hypomanic episodes.

The DSM-IV 4 days minimum duration of hypomania for bipolar II diagnosis was not adhered to. Instead, ≥ 2 days of hypomania was sufficient for bipolar II diagnosis, on the basis of converging data in the literature: the modal range duration of hypomania is reported to be 1–3 days (Akiskal, 1996; Angst, 1998; Akiskal et al., 2000); the Research Diagnostic Criteria (RDC, Spitzer et al., 1978) setting for the minimum duration of hypomania is between 1 and 3 days; a positive family history for bipolar disorder (Akiskal et al., 1977; Cassano et al., 1992); and significant diagnostic stability during long-term follow-up of RDC bipolar II with duration of hypomania of at least 2 days (Coryell et al., 1995).

Most bipolar II patients have more than one hypomanic episode (increasing the reliability of diagnosis; Akiskal et al., 2000). It is important for family members or close friends to supplement the clinical information provided by patient interview (to increase the cross-validated yield of bipolar II diagnosis; Akiskal et al., 2000). These diagnostic features, which were useful in the conduct of the present investigation, are insufficiently emphasized in the SCID.

One further change critical to the present investigation was made to the SCID-CV interview. If the patient's answer to the screening question about past hypomanic episodes ('a period of elevated or irritable mood') was negative, instead of going to the assessment of dysthymic disorder (as required by the SCID-CV skip-out instruction), the patient was always questioned about all the other DSM-IV non-mood manic/hypomanic symptoms. This kind of probing could sometimes lead patients (and also family members or close friends) to remember past episodes of hypomanic behavior (usually with overactivity, increased pleasurable activities, and talkativeness). Then, once an episode of past hypomanic behavior was remembered, often patients and informants remembered that mood was elevated or irritable during that episode (when at the first screening question on hypomanic mood the answer had been negative). Upon re-questioning, only when mood change was admitted—not just that of hypomanic behavioural change—was the confident diagnosis of hypomania made in the present study.

Bipolar II and unipolar MDD were compared on key clinical variables reported to distinguish bipolar from unipolar disorders (Akiskal et al., 2000; Perugi et al., 1998): age at onset, recurrence (more than three MDEs), and atypical features. Age at onset was defined as the earliest age at which an episode met MDE criteria (a highly reliable onset index; McMahon et al., 1994). The bipolar II sample of the present study was also compared with the bipolar II sample of the first author's previous study (Benazzi and Rihmer, 2000), who were interviewed following the SCID-CV skip-out instruction of the screening question on manic-hypomanic mood, and who had at least some days of hypomania as in the present study. The methods of the two studies were identical, except for the change made to the SCID-CV skip-out of the mood item on hypomania.

Means were compared with the *t*-test, and proportions with the two sample test of proportion (STATA 5 statistical software, Stata Corporation, College Station, TX, USA). *P* values were two-tailed, and the probability level was $P < 0.05$.

3. Results

The prevalence of bipolar II was 61.3% (103/168). Comparisons between bipolar II and unipolar are presented in Table 1. Bipolar II had significantly

Table 1
Comparisons between unipolar (UP) and bipolar II (BP)

Variable	UP ($n = 65$)	BP ($n = 103$)	T/Z	DF	*P*
Age (years), mean (S.D.)	47.7 (15.7)	42.0 (14.3)	2.4	166	0.0165
Age at onset (years), mean (S.D.)	30.3 (13.0)	25.5 (12.9)	2.3	166	0.0204
Female gender (%)	60.0	66.0	0.7		0.4309
More than three major depressive episodes (%)	60.0	78.6	2.5		0.0094
Major depressive episodes with atypical DSM-IV features (%)	16.9	47.5	4.0		0.0000

Table 2
Comparisons between bipolar II (BP) of the present study and bipolar II of the author's previous study

Variable	BP ($n = 251$)	BP ($n = 103$)	T/Z	DF	*P*
Age (years), mean (S.D.)	41.7 (13.7)	42.0 (14.3)	0.1	352	0.8535
Age at onset (years), mean (S.D.)	25.7 (11.6)	25.5 (12.9)	0.1	352	0.8867
Female gender (%)	70.5	66.0	0.8		0.4049
More than three major depressive episodes (%)	77.8	78.6	0.1		0.8688
Major depressive episodes with atypical DSM-IV features (%)	45.4	47.5	0.3		0.7188

lower age, lower age at onset, more recurrences, and more atypical features.

Comparisons between the present study bipolar II and the bipolar II of the first author's previous study are presented in Table 2. No significant differences were found: the two data sets were essentially identical.

4. Discussion

The 61% prevalence of bipolar II found in the present study is higher than the top prevalence reported in the literature (Akiskal et al., 2000), and higher than the 45% bipolar II prevalence of the first author's previous study following the strict SCID-CV (Benazzi and Rihmer, 2000). The 16% bipolar II prevalence difference between the two studies is similar to the bipolar II prevalence difference reported by Dunner and Tay (1993) when comparing a semistructured and a structured interview for hypomania. The results are supported by a study reporting that bipolar spectrum disorders are very common (60%), and that many major depressive patients (56%) were found to be bipolar, in a primary care psychiatric setting, when patient assessment was made by trained clinicians carrying out a systematic and careful interview of past hypomania (Ghaemi et al., 2000). The results are further supported by a study showing that 40% of 'unipolar' patients were found to be bipolar after a clinical interview with a checklist of DSM-IV criteria, and with the assessment also based on information from family and other key informants (Ghaemi et al., 1999).

To test the clinical validity of bipolar II in the present study (that is, if they were 'really' bipolar II), key clinical variables reported to distinguish bipolar and unipolar (age at onset, recurrence, atypical features) were compared between the present study bipolar II and unipolar, and between the present study bipolar II and the first author's previous sample of bipolar II. Bipolar II patients in the present study were significantly different from unipolar patients, and were not significantly different from the previous bipolar II sample, thereby supporting the clinical validity of assigning a bipolar II diagnosis to the present cohort of patients interviewed with the skip-out methodology for the stem mood question on hypomania.

The results suggest that a systematic interview of depressed outpatients for past hypomania, using the SCID-CV but not following its mood screening

question skip-out instruction, can increase bipolar II case findings. In the SCID-CV, if the screening question on hypomanic mood is negative, the interviewer cannot assess all the other hypomanic symptoms, but must move on to the assessment of another disorder. The present study shows that assessment of all non-mood hypomanic symptoms (even when the answer to the mood screening question was initially negative) could lead patients to remember periods of hypomanic behavior. When the hypomanic behavior is remembered, patients often remember that mood was also hypomanic during the period in question (when at initial screening they had not remembered a period of hypomanic mood). Hypomanic behavior may be easier to remember—and be noticed by others—than a marked departure of mood from baseline. Of historical note, Akiskal et al. (1977) were the first to stress the importance of hypomanic *behavior* for the diagnosis of hypomania, even if patients denied mood swings.

The findings of the present study have important treatment implications, since a missed bipolar II diagnosis may lead to overuse of antidepressants (which may worsen the course of bipolar disorder by inducing hypomania, rapid cycling and mixed states; Akiskal and Mallya, 1987; Wehr and Goodwin, 1987; Benazzi, 1997b; Akiskal et al., 2000; Ghaemi et al., 2000), and lack of the protective use of mood stabilizers.

The methodological advantages of the present study include a large bipolar II sample, the inclusion of outpatients only, no substance and personality disorders, and a non-academic setting, as mood disorder patients in academic centers may not be representative of typical mood disorder patients. The limitations of the present study include a single interviewer, and cross-sectional assessment. A senior mood disorder clinical and research psychiatrist, collateral information from family members or close friends, standard assessment of consecutive patients, and a systematic interview about past hypomania may have reduced these limitations.

Admittedly, the best external validating strategy for bipolarity is a family history of bipolar disorder. A shorter duration for hypomania when diagnosing bipolar II has been extensively documented in the literature (see Akiskal et al., 2000). What is more critical to the present analysis is the study of Rice et al. (1986) from the NIMH collaborative study, showing that, once the history of hypomania has been documented, it constitutes near perfect external validation for the bipolar nature of depression from a familial bipolar standpoint. We therefore submit that the strict procedures of SCID-CV for hypomania should be liberalized to permit the obtainment of a greater and more reliable yield of hypomanic symptomatology as indicated by our data. Replications for other clinical samples with a blind methodology are desirable.

References

Akiskal, H.S., Djenderedjian, A.M., Rosenthal, R.H., Khani, M.K., 1977. Cyclothymic disorder: validating criteria for inclusion in the bipolar affective group. Am. J. Psychiatry 134, 1227–1233.

Akiskal, H.S., Rosenthal, R.H., Rosenthal, T.L., Kashgarian, M., Khani, M.K., Puzantian, V.R., 1979. Differentiation of primary affective illness from situational, symptomatic, and secondary depressions. Arch. Gen. Psychiatry 36, 635–643.

Akiskal, H.S., Mallya, G., 1987. Criteria for the 'soft' bipolar spectrum: treatment implications. Psychopharmacol. Bull. 23, 68–73.

Akiskal, H.S., 1996. The prevalent clinical spectrum of bipolar disorders: beyond DSM-IV. J. Clin. Psychopharmacol. 16 (Suppl. 1), 4S–14S.

Akiskal, H.S., Pinto, O., 1999. The evolving bipolar spectrum: prototypes I, II, III, and IV. Psychiatr. Clin. North Am. 22, 517–534.

Akiskal, H.S., Bourgeois, M.L., Angst, J., Post, R., Moller, H.-J., Hirschfeld, R., 2000. Re-evaluating the prevalence and diagnostic composition within the broad clinical spectrum of bipolar disorders. J. Affect. Disord. 59 (Suppl. 1), S5–S30.

Angst, J., 1998. The emerging epidemiology of hypomania and bipolar II disorder. J. Affect. Disord. 50, 143–151.

Baldessarini, R.J., 2000. A plea for integrity of the bipolar disorder concept. Bipolar Disord. 2, 3–7.

Benazzi, F., 1997a. Prevalence of bipolar II disorder in outpatient depression: a 203-case study in private practice. J. Affect. Disord. 43, 163–166.

Benazzi, F., 1997b. Antidepressant-associated hypomania in outpatient depression: a 203-case study in private practice. J. Affect. Disord. 46, 73–77.

Benazzi, F., Rihmer, Z., 2000. Sensitivity and specificity of DSM-IV atypical features for bipolar II disorder diagnosis. Psychiatry Res. 93, 257–262.

Benazzi, F., 2000. Borderline personality disorder and bipolar II disorder in private practice depressed outpatients. Comp. Psychiatry 41, 106–110.

Brugha, T.S., Bebbington, P.E., Jenkins, R., Meltzer, H., Taub, N.A., Janas, M., Vernon, J., 1999a. Cross validation of a

general population survey diagnostic interview: a comparison of CIS-R with SCAN ICD-10 diagnostic categories. Psychol. Med. 29, 1029–1042.

Brugha, T.S., Bebbington, P.E., Jenkins, R., 1999b. A difference that matters: comparisons of structured and semi-structured psychiatric diagnostic interviews in the general population. Psychol. Med. 29, 1013–1020.

Cassano, G.B., Akiskal, H.S., Savino, M., Musetti, L., Perugi, G., Soriani, A., 1992. Proposed subtypes of bipolar II and related disorders: with hypomanic episodes (or cyclothymia) and with hyperthymic temperament. J. Affect. Disord. 26, 127–140.

Coryell, W., Endicott, J., Maser, J.D., Keller, M.B., Leon, A.C., Akiskal, H.S., 1995. Long-term stability of polarity distinctions in the affective disorders. Am. J. Psychiatry 152, 385–390.

Coryell, W., 1999. Bipolar II disorder: the importance of hypomania. In: Goldberg, J.F., Harrow, M. (Eds.), Bipolar Disorders. Course and Outcome. American Psychiatric Press, Washington, DC, pp. 219–236.

Dunner, D.L., Tay, L.K., 1993. Diagnostic reliability of the history of hypomania in bipolar II patients and patients with major depression. Comp. Psychiatry 34, 303–307.

Dunner, D.L., 1996. Bipolar depression with hypomania (bipolar II). In: Widiger, T.A., Frances, A.J., Pincus, H.A., Ross, R., First, M.B., Davis, W.W. (Eds.). DSM-IV Sourcebook, Vol. 2. American Psychiatric Association, Washington, DC, pp. 53–63.

Dunner, D.L., 1998. Diagnostic revisions for DSM-IV. In: Goodnick, P.L. (Ed.), Mania. Clinical and Research Perspectives. American Psychiatric Press, Washington, DC, pp. 3–10.

First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B.W., 1997. Structured Clinical Interview For DSM-IV Axis I Disorders—Clinician Version (SCID-CV). American Psychiatric Press, Washington, DC.

Ghaemi, S.N., Sachs, G.S., Chiou, A.M., Pandurangi, A.K., Goodwin, F.K., 1999. Is bipolar disorder still underdiagnosed? Are antidepressants overutilized? J. Affect. Disord. 52, 135–144.

Ghaemi, S.N., Boiman, E.E., Goodwin, F.K., 2000. Diagnosing bipolar disorder and the effect of antidepressants: a naturalistic study. J. Clin. Psychiatry 61, 804–808.

Goldberg, J.F., Kocsis, J.H., 1999. Depression in the course of bipolar disorder. In: Goldberg, J.F., Harrow, M. (Eds.), Bipolar Disorders. Clinical Course and Outcome. American Psychiatric Press, Washington, DC, pp. 129–147.

Hantouche, E.G., Akiskal, H.S., Lancrenon, S., Allilaire, J.-F., Sechter, D., Azorin, J.-M., Bourgeois, M., Fraud, J.-P., Chatenet-Duchene, L., 1998. Systematic clinical methodology for validating bipolar-II disorder: data in mid-stream from a French national multi-site study. J. Affect. Disord. 50, 163–173.

Kessler, R.C., McGonagle, K.A., Zhao, S., Nelson, C.B., Hughes, M., Eshleman, S., Wittchen, H.U., Kendler, K.S., 1994. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the national comorbidity survey. Arch. Gen. Psychiatry 51, 8–19.

Manning, J.S., Haykal, R.F., Connor, P.D., Akiskal, H.S., 1997. On the nature of depressive and anxious states in a family practice setting: the high prevalence of bipolar II and related disorders in a cohort followed longitudinally. Comp. Psychiatry 38, 102–108.

McMahon, F.J., Stine, C., Chase, G.A., Meyers, D.A., Simpson, S.G., DePaulo, J.R., 1994. Influence of clinical subtype, sex, and lineality on age at onset of major affective disorder in a family sample. Am. J. Psychiatry 151, 210–215.

Perugi, G., Akiskal, H.S., Lattanzi, L., Cecconi, D., Mastrocinque, C., Patronelli, A., Vignoli, S., 1998. The high prevalence of soft bipolar (II) features in atypical depression. Comp. Psychiatry 39, 63–71.

Regier, D.A., Boyd, J.H., Burke, J.D., Rae, D.S., Myers, J.K., Kramer, M., Robins, L.N., George, L.K., Karno, M., Locke, B.Z., 1988. One-month prevalence of mental disorders in the United States. Based on five epidemiologic catchment area sites. Arch. Gen. Psychiatry 45, 977–986.

Rice, J.P., McDonald-Cott, P., Endicott, J., Coryell, W., Grove, W.M., Keller, M.B., Altis, D., 1986. The stability of diagnosis with an application to bipolar II disorder. Psychiatry Res. 19, 285–296.

Spitzer, R.L., Endicott, J., Robins, E., 1978. Research Diagnostic Criteria (RDC) For a Selected Group of Functional Disorders, 3rd Edition. New York State Psychiatric Institute, Biometrics Research, New York.

Steiner, J.L., Tebes, J.X., Sledge, W.H., Walker, M.L., 1995. A comparison of the structured clinical interview for DSM-III-R and clinical diagnoses. J. Nerv. Ment. Dis. 183, 365–369.

Wehr, T.A., Goodwin, F.K., 1987. Can antidepressants cause mania and worsen the course of affective illness? Am. J. Psychiatry 144, 1403–1411.