

## SHORT COMMUNICATION

Franco Benazzi

**Depression with DSM-IV atypical features:  
a marker for bipolar II disorder**

Received: 18 February 1999 / Accepted: 29 October 1999

**Abstract** The aim of the study was to find the prevalence of atypical features in bipolar II depression versus unipolar depression. Five hundred and fifty seven unipolar and bipolar II depressed outpatients were interviewed with the Structured Clinical Interview for DSM-IV, the Montgomery Asberg Depression Rating Scale, and the Global Assessment of Functioning Scale. DSM-IV atypical features were significantly more common in bipolar II patients than in unipolar patients (45.4% vs 25.4%, odds ratio 2.4). As the diagnosis of bipolar II disorder is often based on diagnosis of past hypomania, which may not be very reliable, depression with atypical features may point to bipolar II disorder diagnosis.

**Key words** Atypical features · Bipolar II disorder · Unipolar disorder · DSM-IV

**Introduction**

The diagnostic validity of atypical depression was based on better response to MAOI than to tricyclic antidepressants (Quitkin et al. 1997), and on latent class analysis (Sullivan et al. 1998). DSM-IV "atypical features" (mood reactivity, weight / appetite increase, hypersomnia, leaden paralysis, interpersonal rejection sensitivity) can be applied to a major depressive episode (MDE) occurring in major depressive, dysthymic, and bipolar disorders (American Psychiatric Association 1994). Mainly unipolar atypical depressed outpatients were studied (Nierenberg et al. 1998). Atypical features, more common in bipolar II than in unipolar depression (American Psychiatric Association 1994; Benazzi 1997a; Akiskal 1996; Hantouche et al. 1998), might be a marker of bipolar II disorder. The diagnosis of bipolar II disorder may be dif-

ficult. Episodes of hypomania rarely lead to treatment, and clinicians must rely on recollections of patients and informants (Coryell 1999). Patients often see hypomania as a period of well-being and do not report it spontaneously (Akiskal 1996). Unless skillfully interviewed, bipolar II depression may be missed (Akiskal 1995a). Bipolar II disorder may be confused with borderline personality disorder (Coryell 1999). Hypomania must be observed by others to increase reliability (Coryell 1999). The few reliability studies yielded mixed results (Coryell 1999). Despite limitations, bipolar II patients had diagnostic stability (Coryell et al. 1995), and a family history different from bipolar I and unipolar patients (Coryell 1999). Diagnosis of bipolar II disorder has important treatment implications: better response to MAOI and SSRI than to tricyclic antidepressants, antidepressant-induced mixed states, rapid cycling, and hypomania, and use of mood stabilizers (Coryell 1999; Akiskal 1996). As cross-sectional diagnosis may be difficult, markers may be useful. Markers of bipolar II disorder were cyclothymic temperament, antidepressant-associated hypomania, family history of bipolar disorder, acute onset, early onset, highly recurrent, seasonal, and chronic depression, and substance abuse (Akiskal 1996; Akiskal et al. 1995b; Hantouche et al. 1998; Coryell et al. 1995; McMahon et al. 1994; Altshuler et al. 1995).

The aim of the present study was to find the prevalence of DSM-IV atypical features in unipolar and bipolar II depressed outpatients, and to find if atypical features could be a marker of bipolar II disorder.

**Materials and methods**

The study was conducted by a senior psychiatrist, Department of Psychiatry, National Health Service, Forlì, Italy, with 16 years of clinical and research work in mood disorders, in his outpatient private practice. The private setting was chosen because it is more representative of mood disorder patients spontaneously seeking psychiatric treatment in Italy, where it is the first or second (after family doctors) line of treatment and where the most severe mood disorder patients are usually seen in the national psychiatric service or in university centers. Mood disorder patients in academic

F. Benazzi (✉)  
Via Pozzetto 17, 48015 Castiglione di Cervia RA, Italy  
e-mail: f.benazzi@fo.nettuno.it,  
Tel.: +39 0335 6191852, Fax: +39 0543 30069

**Table 1** Comparisons between bipolar II (BII) and unipolar (U) patients

Variable	BII(n 251)	U(n 306)	t/z	df	p
Age, mean (SD) (y)	41.7 (13.7)	48.2 (15.7)	-5.14	555	0.0000
Female gender (%)	70.5	63.0	1.86		0.0623
MADRS, mean (SD)	27.7 (9.0)	28.2 (9.9)	-0.61	555	0.5370
GAF, mean (SD)	55.7 (8.4)	55.1 (9.4)	0.78	555	0.4322
Atypical features (%)	45.4	25.4	4.94		0.0000

centers may not be representative of typical mood disorder patients (Goldberg and Kocsis 1999). Five hundred and fifty seven consecutive outpatients, presenting for treatment of a major depressive episode (MDE), occurring in major depressive and dysthymic disorders (unipolar), and in bipolar II disorder, were included in the study during the last three years. Neither substance abuse nor severe personality disorder patients were included, because they are rare in private practice (Benazzi 1997a, b; Benazzi 1999a-d; Benazzi in press), and to make bipolar II disorder diagnosis more reliable (these disorders may be associated / confused with bipolar II disorder) (Akiskal 1996; Akiskal 1995a). Bipolar I patients were not included because they are rare in private practice in Italy (Benazzi 1997a). MDE with atypical features was defined according to DSM-IV. Patients were interviewed by the author during the first visit with the Structured Clinical Interview for DSM-IV Axis I Disorders-Clinician Version (SCID-CV) (First et al. 1997). The Montgomery and Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg 1979) and the Global Assessment of Functioning (GAF) Scale (American Psychiatric Association 1994) were used to assess MDE severity. As the MADRS does not cover most atypical features, the GAF was also used to assess MDE severity. Often, family members or close friends supplemented the clinical information during the interview.

Means were compared with the t test, and proportions with the two-sample test of proportion (STATA 5 statistical software). All p values were two-tailed, and the probability was  $p < 0.01$ , to reduce type I error (Rothman 1986).

The study was approved by the ethics committee, and it was performed in accordance with the 1964 Declaration of Helsinki. All persons gave informed consent prior to inclusion in the study.

## Results

Among 557 consecutive unipolar and bipolar II patients, 251 (45.0%) were bipolar II and 306 (54.9%) were unipolar. Comparisons between bipolar II and unipolar patients are presented in Table 1. Age was significantly lower in bipolar II patients. Gender and MDE severity were not significantly different. Atypical features were significantly more common in bipolar II patients (odds ratio 2.43,  $X^2 = 23.36$ ,  $df = 1$ ,  $p < 0.0001$ , 95% confidence interval 1.70 to 3.47).

## Discussion

DSM-IV atypical features were significantly more common in bipolar II than in unipolar depressed patients (45% vs 25%, odds ratio 2.4). As diagnosis of past hypomania may not be very reliable (Dunner and Tay 1993), atypical features may support bipolar II disorder diagnosis, being frequent in this disorder. A depression with DSM-IV atypical features may be two times more likely to be bipolar II than unipolar. This finding was not previously re-

ported for DSM-IV atypical features. The large sample makes estimation of proportions more precise.

Some limitations of the present study need to be discussed. The study was based on an outpatient sample of moderate severity. There was a single interviewer, and assessment was non-blind and cross-sectional. Because all assessments were carried out by a single clinician, the validity of the results may be challenged. A bias of the clinician towards the use of certain diagnostic categories might artificially enhance or reduce the prevalence of atypical features in bipolar II disorder. Neither substance abuse nor severe personality disorder patients were included, making the sample less representative, but making bipolar II disorder diagnosis more reliable (Akiskal 1996, 1995a). Phenomenologically, hypomania shades into mania, and DSM-IV differential diagnosis depends on severity. Bipolar II patients are unlikely to present for treatment of hypomania (Coryell et al. 1995) or to report hypomania (Akiskal 1996; McMahon et al. 1994). The distinction between unipolar and bipolar II disorders is often retrospective, limiting reliability (Dunner and Tay 1993). Unless skillfully questioned about past hypomania, bipolar II depression can be missed (Akiskal et al. 1995b). Use of a validated structured interview by a psychiatrist with clinical and research work on mood disorders (Benazzi 1997a, b, 1998a, b, 1999a-d; Benazzi in press), family members or close friends supplementing the clinical information, standard assessment of all patients, and systematic questioning about past hypomania may have reduced these limitations (Akiskal 1996; Akiskal et al. 1995b).

Some advantages of the study were inclusion of outpatients only (making it comparable with most previous clinical studies), an on-academic setting, use of DSM-IV definition of atypical depression, and inclusion of a large number of bipolar II patients (not well studied in previous reports on atypical depression).

## References

- Akiskal HS (1996) The prevalent clinical spectrum of bipolar disorders: beyond DSM-IV. *J Clin Psychopharmacol* 16 (Suppl 1): 4S-14S
- Akiskal HS (1995a) Mood disorders: clinical features. In: Kaplan HI, Sadock BJ (eds) *Comprehensive textbook of psychiatry*. VI ed. Williams & Wilkins, Baltimore, Maryland, pp 1123-1152
- Akiskal HS, Maser JD, Zeller PJ, Endicott J, Coryell W, Keller M, Warshaw M, Clayton P, Goodwin F (1995b) Switching from "unipolar" to bipolar II. An 11-year prospective study of clinical and temperamental predictors in 559 patients. *Arch Gen Psychiatry* 52: 114-123

- Altshuler LL, Post RM, Leverich GS, Mikalauskas K, Rosoff A, Ackerman L (1995) Antidepressant-induced mania and cycle acceleration: a controversy revisited. *Am J Psychiatry* 152: 1130–1138
- American Psychiatric Association (1994) Diagnostic and statistical manual of mental disorders, fourth ed. American Psychiatric Association, Washington, DC
- 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 (1998a) Chronic depression: a case series of 203 outpatients treated at a private practice. *J Psychiatry Neurosci* 23: 51–55
- Benazzi F (1998b) Late-life depression in private practice depressed outpatients: a 203-case study. *Int J Geriatr Psychiatry* 23: 181–182
- Benazzi F (1999a) Atypical depression in private practice depressed outpatients: a 203-case study. *Compr Psychiatry* 40: 80–83
- Benazzi F (1999b) Prevalence and clinical features of atypical depression in depressed outpatients: a 467-case study. *Psychiatry Res* 86: 259–265
- Benazzi F (1999c) Bipolar versus unipolar psychotic outpatient depression. *J Affect Disord* 55: 63–66
- Benazzi F (1999d) Is atypical depression a moderate severity depression? A 536-case study. *J Psychiatry Neurosci* 24: 244–247
- Benazzi F (2000) Bipolar II depression in late life: prevalence and clinical features in 525 depressed outpatients. *J Affect Disord* (in press)
- Coryell W (1999) Bipolar II disorder: the importance of hypomania. In: Goldberg JF, Harrow M (eds) *Bipolar disorders. Clinical course and outcome*. American Psychiatric Press, Washington DC, pp 219–236
- Coryell W, Endicott J, Maser JD, Keller M, Leon AC, Akiskal HS (1995) Long-term stability of polarity distinctions in the affective disorders. *Am J Psychiatry* 152: 385–390
- Dunner DL, Tay KL (1993) Diagnostic reliability of the history of hypomania in bipolar II patients and patients with major depression. *Compr Psychiatry* 34: 303–307
- First MB, Spitzer RL, Gibbon M, Williams JBW (1997) *Structured Clinical Interview for DSM-IV Axis I Disorders-Clinician Version (SCID-CV)*. American Psychiatric Press, Washington, DC
- Goldberg JF, Kocsis JH (1999) Depression in the course of bipolar disorder. In: Goldberg JF, Harrow M (eds) *Bipolar disorders. Clinical course and outcome*. American Psychiatric Press, Washington DC, pp 129–147
- Hantouche EG, Akiskal HS, Lancrenon S, Allilaire JF, Sechter D, Azorin JM, Bourgeois M, Fraud JP, 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
- McMahon FJ, Stine C, Chase GA, Meyers DA, Simpson SG, Depaulo JR (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
- Montgomery SA, Asberg M (1979) A new depression scale designed to be sensitive to change. *Br J Psychiatry* 134: 382–389
- Nierenberg AA, Alpert JE, Pava J, Rosenbaum JF, Fava M (1998) Course and treatment of atypical depression. *J Clin Psychiatry* 59 (Suppl 18): 5–9
- Quitkin FM, Stewart JW, McGrath PJ, Nunes EV, Klein DF (1997) The identification and validation of distinct depressive syndromes in a population-based sample of female twins. *Arch Gen Psychiatry* 54: 970–972
- Rothman KJ (1986) *Modern epidemiology*. Little, Brown and Company, Boston
- Sullivan PF, Kessler RC, Kendler KS (1998) Latent class analysis of lifetime depressive symptoms in the national comorbidity survey. *Am J Psychiatry* 155: 1398–1406