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Prevalence of bipolar II disorder in atypical depression

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Abstract The diagnostic validity of atypical depression is based on its superior response to monoamine oxidase inhibitors compared to tricyclic antidepressants, and on latent class analysis. The studies on atypical depression have often not included bipolar patients. The aim of the present study was to find the prevalence of bipolar II disorder among DSM-IV atypical depression outpatients. Bipolar II and unipolar atypical depressions were also compared to find if they were variants of the same disorder or if instead they were different disorders. One hundred and forty consecutive unipolar and bipolar II outpatients, presenting for treatment of an atypical major depressive episode, were interviewed with the Structured Clinical Interview for DSM-IV, the Montgomery Asberg Depression Rating Scale (MADRS), and the Global Assessment of Functioning Scale. The prevalence of bipolar II disorder was 64.2%. The age at baseline and onset were significantly lower in bipolar II versus unipolar patients. All the other variables (MADRS items, duration of illness, severity, gender, psychosis, comorbidity, chronicity, recurrences) were not significantly different. The prevalence of bipolar II disorder among atypical depressed outpatients was higher than previously reported.

Key words Atypical depression · Bipolar II disorder · Unipolar disorder · Outpatients

Introduction

According to the DSM-IV (American Psychiatric Association, 1994), atypical depression is a major depressive episode with atypical features, occurring in major depressive/bipolar I/II disorders, or a dysthymic disorder with atypical features. The diagnostic validity of atypical depression is based on its superior response to monoamine oxidase inhibitors compared to tricyclic antidepressants (Lam and Stewart, 1996; Quitkin et al., 1997) and on latent class analysis (Kendler et al., 1996). Clinical studies on atypical depression have often not included bipolar patients (Davidson et al. 1982; Paykel et al., 1983; Liebowitz et al., 1984; Horwath et al., 1992). Some studies (not designed to find the prevalence of bipolar II disorder) have reported a past history of hypomania in 10%–11% of atypical depressed outpatients (Stewart et al., 1997; McGrath et al., 1992; Quitkin et al., 1991; Quitkin et al., 1989). A recent study (Perugi et al., 1998), has reported a prevalence of DSM-IV bipolar II disorder of 32.5% and of bipolar spectrum disorders of 39.5% among 86 atypical depressed in-outpatients. This apparent rising prevalence of bipolar II disorder among atypical depressed patients may be related to the structured, systematic questioning about past hypomanic episodes (Akiskal, 1996). The concurrent interview of family members may also increase bipolar II case findings, as these patients tend to underreport hypomanic episodes, which they see as periods of well being (Akiskal, 1995; Goodwin and Jamison, 1990). The aim of the present study was to find the prevalence of bipolar II disorder among DSM-IV atypical major depressive episode outpatients. Another aim was to compare bipolar II with unipolar atypical depression to find if they were variants of the same disorder or if instead they were different disorders.

Methods

The study was carried out in the outpatient general psychiatry private practice by a senior psychiatrist of the Department of Psychiatry of the Public Hospital of Forlì (Italy), with a 15-year experience in the diagnosis and treatment of mood disorders (more than 4000 personal visits/year, more than 400 new patients/year). The private setting is more representative of mood disorder patients spontaneously seeking psychiatric treatment in Italy, where the public setting deals mainly with the most severe patients. One hundred and forty consecutive outpatients, presenting for treatment of a DSM-IV major depressive episode with atypical features, occurring in major depressive and dysthymic disorders (unipolar depression), and in bipolar II disorder (bipolar II depression), with or without concurrent psychopharmacological treatment, were in-

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Table 1 Comparisons between atypical bipolar II (BII) and atypical unipolar (U) depression

Variables	BII (n = 90)	U (n = 50)	
Age at baseline (y) [mean (SD)]	36.7 (11.1)	44.5 (16.1)	t = 3.40 df = 138 p = 0.0009
Age at onset first major depressive episode (y) [mean (SD)]	24.1 (9.1)	29.9 (15.1)	t = 2.84 df = 138 p = 0.0052
Duration of illness (y) [mean (SD)]	12.9 (10.3)	14.8 (10.8)	t = 1.20 df = 138 p = 0.2309
Baseline MADRS [mean (SD)]	27.9 (6.9)	27.8 (8.5)	t = 0.04 df = 138 p = 0.9681
Baseline GAF [mean (SD)]	55.6 (7.0)	54.4 (9.2)	U = 2178 p = 0.7522
Female gender (%)	81.1	70.0	X2 = 1.66 df = 1 p = 0.1970
Psychotic features (%)	1.1	10.0	Fisher's exact p = 0.0200
Axis I comorbidity (%)	71.1	74.0	X2 = 0.02 df = 1 p = 0.8661
Chronic/without full interepisode recovery major depressive episode (%) (> 2 years)	35.5	54.0	X2 = 3.76 df = 1 p = 0.0525
More than three major depressive episodes (%)	78.8	68.0	X2 = 1.49 df = 1 p = 0.2217

cluded during the last 2 years. The DSM-IV atypical features were 1) mood reactivity, 2) two or more of the following: weight gain or appetite increase, hypersomnia, leaden paralysis, interpersonal rejection sensitivity, and 3) no melancholic or catatonic features. Substance abuse, severe personality disorder, and bipolar I patients were not included, because they are rarely seen in private practice (Benazzi 1997 a, b). As the modal duration of a hypomanic episode has been reported to be 1–3 days (Akiskal, 1996), the DSM-IV 4 days minimal duration of hypomania was not included. Instead, "at least some days" of hypomania were required. As the bipolar II patients did not meet the full DSM-IV criteria, many "soft" bipolar II patients were included. Patients were interviewed by the author 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). The MADRS does not cover most atypical symptoms, but the GAF gives a global measure of severity, and it overcomes the need to score individual symptoms. Often, family members supplemented the clinical information during the interview. Axis I comorbid disorders were recorded when they were reported by the patients, without systematic probing, after SCID-CV interview.

This approach may have led to underreporting, but not to a differential misclassification related to information bias, because the sample was large, and because there was no reason to think that one group of patients was more likely than the other to report comorbid disorders. The significance of the difference between means was tested with the t test, or with the Mann Whitney U test for data not normally distributed at the Kolmogorov-Smirnov test. The significance of the difference between proportions was tested with the Chi-square test, or with the Fisher's exact test for small frequencies. All p values were two-tailed. A probability level of 0.01 was chosen to reduce the risk of type I error due to multiple comparisons, without increasing too much the risk of type II error.

The study was performed in accordance with the 1964 Declaration of Helsinki, and all patients gave informed consent prior to inclusion in the study.

Results

The prevalence of bipolar II disorder among atypical depressed patients was 64.2% (90/140). The comparisons between the bipolar II and the unipolar patients are presented in Table 1. The age at baseline and the age at onset of the first major depressive episode were significantly lower in bipolar II patients. All the other variables (duration of illness, severity, female gender, psychosis, comorbidity, chronicity, recurrences) were not significantly different. The comparisons of the scores of the MADRS items between the bipolar II and the unipolar patients are presented in Table 2. No significant differences were found.

Table 2 Comparisons of MADRS item scores between atypical bipolar II (BII) and atypical unipolar (U) depression (Mann Whitney U test)

MADRS item score [mean (SD)]	BII	U	U test	p
Apparent sadness	3.0 (1.2)	3.2 (1.3)	2134	0.6112
Reported sadness	3.3 (1.2)	3.4 (1.2)	2116	0.5578
Inner tension	3.4 (0.9)	3.4 (1.0)	2142	0.6346
Reduced sleep	2.0 (2.0)	2.0 (2.0)	2227	0.9199
Reduced appetite	0.6 (1.2)	0.5 (1.1)	2223	0.9044
Concentration difficulties	3.2 (1.3)	3.3 (1.5)	2163	0.7048
Lassitude	3.6 (1.4)	3.5 (1.6)	2208	0.8538
Inability to feel	3.6 (1.5)	3.6 (1.5)	2207	0.8504
Pessimistic thoughts	3.5 (1.0)	3.4 (1.3)	2181	0.7620
Suicidal thoughts	1.3 (1.1)	1.1 (1.3)	2022	0.3192

Discussion

The results of this study support the findings of a previous study (Perugi et al., 1998), reporting a high prevalence of bipolar II disorder among atypical depressed patients. In the present study, a higher prevalence of bipolar II disorder was found (64.2% vs 32.5%). This finding may be related to the exclusion of the DSM-IV threshold of 4 days of hypomania (with the consequent inclusion of many "soft" bipolar II patients), to the concurrent interview of family members, and to the structured, systematic questioning about past hypomanic episodes. As the DSM-IV minimal duration of hypomania was not included, the real prevalence of DSM-IV bipolar II disorder was not detected in the present study, and it may be assumed that the prevalence is lower when the full DSM-IV criteria are used. In another study (Robertson et al., 1996) comparing atypical features between bipolar and unipolar depression (the only one found on a MEDLINE search in addition to that of Perugi et al.), no difference in the prevalence of

atypical depression was reported. This finding is not confirmed by the present study nor by that of Perugi et al. This difference with Robertson et al.'s results may be related to the use, in that study, of full DSM-IV criteria for hypomania, to the inclusion of many bipolar I patients (not included in the present study), to the small sample of bipolar patients (20 bipolar I, 10 bipolar II), and to the inclusion of inpatients. As in the study of Perugi et al., no significant differences were found on gender, duration, recurrences, chronicity, severity, axis I comorbidity, and symptomatological features between bipolar II and unipolar atypical patients. In addition, psychosis prevalence was not significantly different. Contrary to the findings of Perugi et al., the age at baseline and the age at onset were significantly lower in bipolar II than in unipolar patients. This different finding may be related to the smaller sample of Perugi et al.'s study (24 unipolar and 28 bipolar II patients), limiting the power to detect significant differences, to the setting (a university setting has usually more severe patients), and to the inclusion of inpatients. As differences in age at onset can differentiate subtypes of disorders caused by different genes (McMahon et al., 1994), the observed different age at onset might support the subdivision of atypical depression into a bipolar II and a unipolar subtype. A subdivision further supported by the presence of hypomania, for its therapeutic implications (antidepressants may induce switches, rapid cycling, and mixed states in bipolar II patients, and mood stabilizers may be used [Akiskal, 1996; Tondo et al., 1998]). However, because the bipolar II patients of the present study did not meet the full DSM-IV criteria, this subdivision should be seen as tentative and requiring replication in samples meeting the full DSM-IV criteria for bipolar II disorder. Some differences reported between bipolar disorders and major depressive disorder (unipolar depression) were not observed in this study between bipolar II and unipolar atypical depression: the female to male ratio near 1 in bipolar I disorder (American Psychiatric Association, 1994; Depression Guideline Panel, 1993), the higher number of recurrences in bipolar I/II disorder (American Psychiatric Association, 1994), the higher comorbidity in bipolar II disorder (Cassano et al.; 1992), and the higher rate of psychosis in bipolar I disorder (Goodwin and Jamison, 1990). These findings may be related to the observation that bipolar II depression without comorbid substance abuse and severe personality disorder does not have more recurrences, more axis I comorbidity, more chronicity, and more psychosis than unipolar depression (Benazzi, 1997 a, b; Cooke et al., 1995). The results of the present study may be limited to samples of depressed outpatients of moderate severity, and they may not apply to samples of more severe outpatients and to inpatients, who are usually seen in university and public settings. The exclusion of substance abuse and severe personality disorder patients may have selected a more homogeneous sample. Due to the exclusion of the DSM-IV minimal duration of hypomania, many "soft" bipolar II patients have been included. In conclusion, "soft" bipolar II disorder seems more common than previously reported in atypical depression.

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