Toward better probing for hypomania of bipolar-II disorder by using Angst's checklist

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ABSTRACT *The reliability of the diagnosis of bipolar-II disorder (BP-II) is still a problem. Semi-structured interviews by clinicians might partly overcome this problem. The aims of this study were to find the degree of agreement in the diagnosis of BP-II between the Structured Clinical Interview for DSM-IV (SCID) and a semi-structured interview based on Angst's hypomania checklist (Angst et al., 2003), and to assess the priority among hypomanic symptoms for the diagnosis of BP-II. Remitted depression outpatients (N = 102) were interviewed during a follow-up visit using the Structured Clinical Interview for DSM-IV (SCID), and then with Angst's semi-structured interview, following DSM-IV criteria. Bipolar I (BP-I) patients were excluded. Using the SCID, 29 patients were diagnosed BP-II, 26 BP-I, and 47 major depressive disorder (MDD). By the semi-structured interview 69 patients were diagnosed BP-II, 33 MDD, and none BP-I. Agreement for the diagnosis of BP-II between the two interviews was 53.9% ($k = 0.18$). Re-analysis, after deleting the SCID question on the impact on functioning (DSM-IV unclear boundary between BP-I and BP-II), increased agreement to 78.4% ($k = 0.55$). Elevated mood and overactivity (increased goal-directed activity) had the lowest agreement ($k = 0.46$ – 0.49). For predicting BP-II, overactivity had the highest sensitivity (94.2%), while elevated mood had a sensitivity of 84.0%. Multivariate analysis for predicting BP-II (diagnosed by semi-structured interview), including all DSM-IV hypomanic symptoms, found that mood change and overactivity were the only independent predictors. Overactivity plus at least three symptoms (as suggested by Angst and Gamma, 2002) were present in 71 patients, of whom 91.5% also met DSM-IV criteria for hypomania. Overactivity and elevated mood were strongly associated (but not overactivity and irritability). Findings may support a diagnosis of BP-II based on Angst's semi-structured interview versus the fully structured SCID interview. While DSM-IV always requires mood change for the diagnosis of hypomania, the present findings may suggest that overactivity could have the same priority, as suggested by Angst et al. (2003) and by Akiskal et al. (1977, 2001, 2003).*

Key words: bipolar II disorder, diagnosis, reliability, SCID, structured interview

Introduction

The diagnosis of bipolar-II disorder (BP-II) could have a low inter-rater reliability according to some studies (Coryell, 1999; Andreasen et al., 1981; Mazure and Gershon, 1979; Keller et al., 1981; Rice et al., 1986). These studies have several limitations, such as the use of fully structured interviews, non-clinician interviewers, and very small samples of BP-II.

Recent studies compared the reliability of the diagnoses of mood disorders between fully structured

interviews and semi-structured interviews by clinicians, finding a low agreement between the two types of interview, and many false negatives (a low sensitivity) using fully structured interviews (Aalto-Setälä et al., 2002; Eaton et al., 2000; Brugha et al., 1999; Helzer et al., 1985). Inter-rater reliability of BP-II diagnosis was high when interviewers were psychiatrists using semi-structured interviews (Dunner and Tay, 1993; Simpson et al., 2002). Supporting these findings is the diagnostic stability

of BP-II (Coryell et al., 1995; Akiskal et al., 1995) when diagnosed by clinicians using semi-structured interviews. Prevalence of BP-II was very different according to the type of interview used. Prevalence ranged between 0.3% and 2.0% (it was around 3.5% for all DSM-IV bipolar disorders) when fully structured interviews were used, usually in community studies (American Psychiatric Association, 2000, 2002; Faravelli and Incerpi, 1985; Stefansson et al., 1991; Oliver and Simmons, 1985; Regier et al., 1990; Heun and Maier, 1993; Weissman et al., 1988, 1996; Levav et al., 1993; Szadoczky et al., 1998; Hirschfeld et al., 2003), while it was around 10% when Angst's semi-structured interview was used (Angst et al., 2003). Frequency of BP-II in depressed outpatients was higher (around 50%) than previously reported when interviewers were clinicians using semi-structured interviews (Hantouche et al., 1998; Perugi et al., 1998; Benazzi and Akiskal, 2003a; Akiskal and Benazzi, 2003; Akiskal et al., 2000; Angst, 1996; Angst et al., 2003).

Another limitation of structured interviews is the presence of a skip-out instruction in the stem question about past episodes of elevated or irritable mood (a negative response requires switching to assessment of a non-bipolar disorder). Instead, a clinician using a semi-structured interview can assess all past hypomanic symptoms, especially overactivity (increased goal-directed activity) (Benazzi and Akiskal, 2003a; Angst et al., 2003). Bypassing this skip-out instruction increased the frequency of BP-II diagnoses by 33% (Benazzi and Akiskal, 2003a; Akiskal and Benazzi, 2003).

Overactivity (an observable behaviour, easier to remember than past mood change) might be more important than mood change for the diagnosis of mania and hypomania, according to some studies (Akiskal et al., 1977, 2001, 2003; Angst et al., 2003; Benazzi and Akiskal, 2003a,b). Factor analysis studies found that overactivity was the core feature of hypomania (and mania) (Benazzi and Akiskal, 2003b; Hantouche et al., 2003; Bauer et al., 1991). Overactivity symptoms were the most common manic/hypomanic symptoms in the review by Goodwin and Jamison (1990). Akiskal et al. (2001) and Angst and Gamma (2002) placed overactivity at the same priority level of mood change for the diagnosis of mania and hypomania (while in DSM-IV

mood change must always be present). Clear descriptions of overactivity can be found in Kraepelin (1921), Hecker (English translation by Koukopoulos, 2003), and Akiskal (2002).

Study aims

To find the degree of agreement in the diagnosis of BP-II between the Structured Clinical Interview for DSM-IV (SCID) (First et al., 1997) and a semi-structured interview based on Angst's checklist for hypomania (Angst et al., 2003). This is the first study comparing these two types of interviewing for the diagnosis of BP-II. Further goals were to get more insight into the structure of hypomania and its diagnostic criteria.

Methods

Study setting

The setting was a general psychiatry outpatient private practice (a University of California at San Diego (USA) collaborating centre). Private practice is more representative of mood disorders in Italy, because

- it is the first or the second (after family doctors) line of treatment of mood disorders;
- the most severe patients are usually seen in university and national mental health services;
- people do not like to be treated for mental problems in national health services for fear of stigma; and
- most people can see a private psychiatrist, reducing a possible bias related to income.

The author's busy private practice is a series of solo offices in different cities of northern Italy. As it is a general psychiatry practice, it is unlikely that it has a concentration of uncommon and/or treatment-resistant patients (as it is instead often the case in tertiary-care settings).

Patient population

Remitted major depressive episode (MDE) outpatients (N = 102) were seen consecutively in 4 weeks. Substance-related and borderline personality disorders patients were excluded, because these disorders can confound the diagnosis of BP-II (Akiskal and Pinto,

1999) and are also rare in the study setting (Benazzi, 2000). Clinically significant general medical illnesses and cognitive disorders patients were excluded.

Study design and assessment instruments

When remitted from depression (with a Global Assessment of Functioning scale (GAF) score of 80 to 90) for at least one month, patients were interviewed about history of manic and hypomanic episodes during a follow-up visit. As BP-II are likely to need closer follow-ups, BP-II were over-represented in this sample.

The interviewer was an expert clinical and research psychiatrist, whose inter-rater agreement for the diagnosis of bipolar disorders had been found to be high (Benazzi, 2003). Patients were first interviewed with the Structured Clinical Interview for DSM-IV (SCID, First et al., 1997), mood disorder module, hypomania and mania section. The SCID II was not used because it was not required for study goals (borderline personality disorder was excluded by clinical evaluation following DSM-IV criteria). The diagnosis of bipolar-I (BP-I) had to be clear-cut to meet study aims, therefore it was based on psychosis during mania, or on hospital admission for mania, according to DSM-IV (and in line with Dunner et al.'s (1976a,b) original distinction between BP-I and BP-II). The DSM-IV also allows a diagnosis of mania if it causes 'marked impairment' (not specified in detail). This last criterion is, however, an unclear boundary between mania and hypomania, which can easily lead to misclassification.

The SCID structured questions for the diagnosis of BP-I and BP-II (which require a yes/no answer) were strictly followed. According to the SCID, the distinction between BP-I and BP-II is based on a single question assessing the DSM-IV 'marked impairment' cut-off: 'at that time did you have serious problems at home or at work because you were (symptoms) or did you have to go into a hospital?'

Then, patients were interviewed with a semi-structured interview based on Angst's checklist for the diagnosis of history of hypomania, requiring clinical evaluation (Angst et al., 2003). Angst's hypomania checklist is a 20-item semi-structured interview, which covers all DSM-IV symptoms of

hypomania. It often has more than one item for each DSM-IV symptom, especially for overactivity. The items about overactivity that were found to be more useful were the following: 'more social activities, overspending, more physical activity (moving about more), more plans and ideas'. If at least one item related to a given symptom was positive, then the symptom was recorded as present. If the episode had psychotic symptoms (specific questions were asked following the SCID psychotic symptoms module), or required hospital admission (always inquired), the diagnosis was of mania and the patient was not included into the study. The time required on average to use the two interviews was around 15 minutes (the interviewer was skilled in the diagnosis of BP-II as he has been systematically interviewing about history of hypomania for 10 years).

Angst's semi-structured interview was used versus the SCID because it may have some benefits compared to the SCID for the diagnosis of BP-II (more questions on overactivity, being semi-structured, requiring clinical evaluation). The present study method was similar to that used by Helzer et al. (1985), when the same clinician first used a structured interview, and soon after that used a semi-structured interview based on diagnostic criteria. Advantages of a semi-structured interview versus the SCID are that 1) no skip-out instruction has to be followed 2) probing can focus more on history of overactivity 3) wording of the questions can be changed to improve and check the understanding by patient and family members/close friends. Mood change was always required for the diagnosis of hypomania, following DSM-IV. This interview method was similar to that followed by Dunner and Tay (1993), who found more correct diagnoses of BP-II compared to the SCID. The present study interviewer balanced the time of each interview, in order not to make one of the two interviews 'disadvantaged'.

The DSM-IV minimum duration of 4 days for the diagnosis of hypomania was not followed, because several studies support a minimum duration of 2 days (Akiskal et al., 1977; Cassano et al., 1992; Coryell et al., 1995; Akiskal, 1996; Angst, 1998; Akiskal et al., 2000; Benazzi, 2001; Simpson et al., 2002; Angst et al., 2003), and because there are no data supporting the DSM-IV 4-days cut-off (Dunner, 1998).

Data analysis

STATA Statistical Software, Release 7, was used (Stata Corporation, College Station, TX, USA, 2001). Logistic regression was used to study associations, sensitivity, specificity, and area under the ROC (Receiver Operating Characteristic) curve. Two-tailed P was used, and alpha level was set at 0.05.

Results

The Structured Clinical Interview for DSM-IV diagnosed 29 patients as BP-II, 26 as BP-I, and 47 as MDD. The semi-structured interview diagnosed 69 patients as BP-II (67.6%), 33 as MDD, and none as BP-I (agreement = 52.9%, $k = 0.18$). As no BP-I was included in the sample, the SCID question on 'marked impairment' could have led to misclassification.

By deleting the question on impairment, 55 patients were diagnosed as BP-II by SCID, leading to an increased agreement of 78.4% ($k = 0.55$). Agreements between each DSM-IV symptom of hypomania diagnosed by the SCID and by the semi-structured interview are presented in Table 1. The lowest kappa-agreement was that for elevated mood and for overactivity. The BP-II sample diagnosed by the semi-structured interview is presented in Table 2.

Overactivity was the most common symptom, and it was more common than elevated mood. Symptoms present in more than 60% of patients were overactivity, elevated mood, irritable mood, increased self-esteem, more talkativeness, and racing thoughts. Overactivity plus at least three hypomanic symptoms (following Angst and Gamma (2002) proposed diagnostic criteria for hypomania) were present in 71

Table 1. Agreement on the diagnosis of individual hypomanic symptoms between SCID interview and semi-structured interview.

HYPOMANIA SYMPTOMS	Agree %	Expected %	Kappa	P
Elevated mood	72.5	48.9	0.46	0.0000
Irritable mood	88.2	51.9	0.75	0.0000
Increased self-esteem	78.4	49.3	0.57	0.0000
Reduced need for sleep	90.2	51.8	0.79	0.0000
More talkativeness	79.4	49.8	0.58	0.0000
Racing thoughts	88.2	56.8	0.72	0.0000
Distractibility	88.2	50.1	0.76	0.0000
Overactivity (increased goal-directed activity)	80.3	61.0	0.49	0.0000
Risky behaviour	90.2	53.5	0.78	0.0000

Table 2. Clinical features of past hypomanic episodes diagnosed by semi-structured interview (n = 69)

Index mean (SD) age (years)	42.9 (11.4)
Female gender %	73.9
Elevated mood %	84.0
Irritable mood %	72.4
Increased self-esteem %	71.0
Reduced need for sleep %	59.4
More talkativeness %	68.1
Racing thoughts %	76.8
Distractibility %	60.8
Overactivity % (increased goal-directed activity)	94.2
Risky behaviour %	43.4
Mean (SD) N symptoms	6.2 (1.2)
>1 episode %	86.9
Increased functioning (i.e., GAF = 100)	65.2%

GAF = global assessment of functioning scale

patients (69.6%), of whom 91.5% also met the criteria for BP-II diagnosis by semi-structured interview. The sensitivity, specificity, and area under the ROC curve of each DSM-IV hypomanic symptom for predicting BP-II are presented in Table 3.

Overactivity had the highest sensitivity (94.2%, while the sensitivity of elevated mood was 84.0%), and its specificity was lower than that of elevated mood (63.6% versus 78.7%). Forward stepwise multiple logistic regression for predicting BP-II (Table 4), including all DSM-IV hypomanic symptoms assessed by semi-structured interview, found that mood change and overactivity were the only independent predictors. Overactivity versus elevated mood had odds ratio = 7.8, 95% confidence interval 2.8 to 21.6, while overactivity versus irritable mood had odds ratio = 2.0, 95% confidence interval 0.8 to 5.0 (non-significant).

Discussion

Agreement between the SCID and the semi-structured interview for the diagnosis of BP-II was low (only 52.9%, $k = 0.18$). This difference might be one of the reasons for the different prevalence rates of BP-II found in many studies (see introduction). This finding is in line with a previous report (Helzer et al., 1985), finding a low kappa-reliability for mood disorders between a structured interview and a semi-structured interview by the same clinician during the same visit (as in the present study). No BP-I was diagnosed by the semi-structured interview, even if this diagnosis could have been made if study criteria for mania had been met. Results are also in line with re-analyses of diagnoses of bipolar disorders of some community studies (see introduction), which used fully structured interviews (Ghaemi et al., 2002).

Table 3. Ability of individual hypomanic symptoms to predict the diagnosis of bipolar-II diagnosed by semi-structured interview (by logistic regression)

HYPOMANIA SYMPTOMS	OR	95% CI	SE %	SP %	ROC
Elevated mood	19.5	6.8 to 56.2	84.0	78.7	0.81
Irritable mood	4.6	1.9 to 11.1	72.4	63.6	0.68
Increased self-esteem	7.6	2.9 to 19.8	71.0	75.7	0.73
Reduced need for sleep	22.6	5.0 to 102.5	59.4	93.9	0.76
More talkativeness	11.9	4.0 to 35.1	68.1	84.8	0.76
Racing thoughts	3.9	1.6 to 9.8	76.8	54.5	0.65
Distractibility	2.7	1.1 to 6.4	60.9	63.6	0.62
Overactivity (increased goal-directed activity)	28.4	8.2 to 97.6	94.2	63.6	0.78
Risky behaviour	5.5	1.7 to 17.5	43.5	87.9	0.65

OR = odds ratio; 95% CI = 95% confidence interval; SE = sensitivity; SP = specificity; ROC = receiver operating characteristic curve

Table 4. Independent predictors of bipolar-II (diagnosed by semi-structured interview) among hypomanic symptoms (by forward stepwise multiple logistic regression [$F(9,92) = 24.6$; $p = 0.0000$]).

HYPOMANIA SYMPTOMS	Coef.	95% CI	T	P
Elevated mood	0.31	0.17 to 0.45	4.4	0.000
Irritable mood	0.17	0.05 to 0.29	2.8	0.005
Increased self-esteem	0.12	0.00 to 0.25	2.0	0.048
Reduced need for sleep	0.09	-0.27 to 0.22	1.5	0.124
More talkativeness	0.12	0.00 to 0.25	2.0	0.047
Racing thoughts	0.12	-0.00 to 0.25	1.9	0.056
Distractibility	0.10	-0.01 to 0.22	1.7	0.090
Overactivity (increased goal-directed activity)	0.28	0.13 to 0.44	3.7	0.000
Risky behaviour	0.11	-0.00 to 0.23	1.93	0.056

Coef. = coefficient; 95% CI = 95% confidence interval

In the present study, agreement improved when the SCID question on impairment was deleted, suggesting that the DSM-IV cut-off criterion 'marked impairment' between BP-I and BP-II might lead to misclassification. However, even then agreement was far from perfect (78.4%, $k = 0.55$). This finding may suggest that the diagnosis of hypomania by structured interview should not require the assessment of 'marked' impairment, because this assessment cannot be done with a single and simple question, but it requires an in-depth evaluation by a clinician. Furthermore, hypomania often has *improved* functioning (Dunner, 1996; Akiskal, 2002; Hecker, English translation by Koukopoulos, 2003; Benazzi, *in press*), which is not reported in DSM-IV diagnostic criteria for hypomania. In line with these reports, in the present study increased functioning was present in many BP-II patients. Interestingly, the lowest kappa agreement was that for elevated mood and for overactivity, which, being two key symptoms of hypomania, could be another reason explaining the low agreement between the SCID and the semi-structured interview for the diagnosis of BP-II in the present study.

Recent psychometric and clinical studies have found that overactivity can be at least as important as mood change for the diagnosis of mania and hypomania (Akiskal et al., 2001; Angst et al., 2003; Hantouche et al., 2003; Benazzi and Akiskal, 2003b). In the present study, overactivity was the most common hypomanic symptom, present in 94.2% of BP-II, and more common than elevated mood (the 'typical' symptom of mania/hypomania, according to the current diagnostic systems, the DSM-IV (American Psychiatric Association, 1994), and the ICD-10 (World Health Organization, 1992)). This finding is in line with the review by Goodwin and Jamison (1990) on the frequencies of manic/hypomanic symptoms. The sensitivity of overactivity for BP-II diagnosed by semi-structured interview was very high (meaning few false negatives), and it was higher than that of elevated mood, supporting the importance of overactivity for the diagnosis of BP-II.

Multivariate analysis showed that, among all DSM-IV, hypomanic symptoms, elevated mood and overactivity were the only strong and independent predictors of BP-II. This finding may further support the suggestion by Angst et al. (2003) and Akiskal et al. (1977, 2001, 2003) to give overactivity the

same priority given by DSM-IV to mood change for the diagnosis of hypomania. Furthermore, elevated mood and overactivity were strongly associated. Instead, no association was found between overactivity and irritable mood.

By using overactivity as a priority symptom for the diagnosis of hypomania, plus at least three symptoms (as suggested by Angst and Gamma, 2002), BP-II was present in 69.6% (of whom 91.5% met DSM-IV criteria for BP-II). Compared to the 67.6% BP-II diagnosed by semi-structured interview according to DSM-IV, giving overactivity priority for the diagnosis of hypomania may not lead to BP-II overdiagnosis. Probing more on history of overactivity than on history of mood change might reduce the reported BP-II underdiagnosis (American Psychiatric Association, 2002; Ghaemi et al., 2002). Based on the frequency data, the most common symptoms of hypomania were overactivity, mood change, increased self-esteem, more talkativeness, and racing thoughts, suggesting that these symptoms may be the core symptoms of hypomania. Overall, the study results suggest that the BP-II patients of this sample were the 'sunny' BP-II described by Hantouche et al. (2003).

Limitations

A single interviewer limited the validity of the findings. However, findings are in line with previous reports done by independent interviewers (see introduction). Findings may be related to the study setting, a non-tertiary care setting. In tertiary-care settings findings may be different, because one might be more likely to find the so-called 'dark' BP-II (BP-II plus cyclothymic temperament, which is an unstable personality trait leading to more relapses and to more impairment of functioning) (Akiskal et al., 2003). Comparison studies are required to support this possible difference related to the setting. Future studies should be based on independent and blind interviewers to confirm the present study results. Inter-rater reliability and test-retest are the basic requirements for validating a questionnaire, especially when questionnaires are used in different languages and contexts. Replication of the results by studies based on larger community, preferably national, samples and investigating varying thresholds for defining a hypomanic syndrome would be necessary to modify or extend the present finding of

a very high prevalence of bipolar spectrum conditions (Angst et al, 2003).

In conclusion

The results of the present study may support the validity of a BP-II diagnosis based on clinical evaluation by using Angst's semi-structured interview for hypomania, versus the fully structured SCID interview. This type of interviewing might reduce the underdiagnosis of BP-II. The importance of overactivity for the diagnosis of hypomania may be supported by the study findings.

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