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Research report

Toward a re-definition of subthreshold bipolarity: epidemiology and proposed criteria for bipolar-II, minor bipolar disorders and hypomania

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Abstract

Background: The boundaries of bipolarity have been expanding over the past decade. Using a well characterized epidemiologic cohort, in this paper our objectives were: (1) to test the diagnostic criteria of DSM-IV hypomania, (2) to develop and validate criteria for the definition of softer expressions of bipolar-II (BP-II) disorder and hypomania, (3) to demonstrate the prevalence, clinical validity and comorbidity of the entire soft bipolar spectrum. *Methods*: Data on the continuum from normal to pathological mood and overactivity, collected from a 20-year prospective community cohort study of young adults, were used. Clinical validity was analysed by family history, course and clinical characteristics, including the association with depression and substance abuse. *Results:* (1) Just as euphoria and irritability, symptoms of overactivity should be included in the stem criterion of hypomania; episode length should probably not be a criterion for defining hypomania as long as three of seven signs and symptoms are present, and a change in functioning should remain obligatory for a rigorous diagnosis. (2) Below that threshold, 'hypomanic symptoms only' associated with major or mild depression are important indicators of bipolarity. (3) A broad definition of bipolar-II disorder gives a cumulative prevalence rate of 10.9%, compared to 11.4% for broadly defined major depression. A special group of minor bipolar disorder (prevalence 9.4%) was identified, of whom 2.0% were cyclothymic; pure hypomania occurred in 3.3%. The total prevalence of the soft bipolar spectrum was 23.7%, comparable to that (24.6%) for the entire depressive spectrum (including dysthymia, minor and recurrent brief depression). *Limitation:* A national cohort with a larger number of subjects is needed to verify the numerical composition of the softest bipolar subgroups proposed herein. *Conclusion:* The diagnostic criteria of hypomania need revision. On the basis of its demonstrated clinical validity, a broader concept of soft bipolarity is proposed, of which nearly 11% constitutes the spectrum of bipolar disorders proper, and another 13% probably represent the softest expression of bipolarity intermediate between bipolar disorder and normality.

Keywords: Epidemiology; Bipolar-II disorder; Minor bipolar disorder; Hypomania; Prevalence; Comorbidity; Validity

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1. Introduction

Although the psychopathology of hypomania was described in great detail in the nineteenth century by Jules Falret (1878, 1879), and the term hypomania coined very soon thereafter by Mendel (1881), it took almost a century to define hypomania operationally, and that definition is still in a state of flux today. Minimum duration, stem criteria, and the number of signs and symptoms are three areas of requiring a good deal more systematic investigation. The minimum duration required for a diagnosis has changed significantly over the years; it was 2 days in the Research Diagnostic Criteria (Spitzer et al., 1978), not specified in DSM-III or DSM-III-R, and 4 days in DSM-IV, and recently a group of bipolar experts recommended to revert back—on the basis of extensive evidence—to the minimum of 2 days (Akiskal et al., 2000). Elevated, expansive or irritable mood, the stem criterion A of DSM-IV mania, has also been questioned, with Akiskal et al. (2001) recently suggesting that activation be considered as a stem criterion, a finding in line with his original recommendation (Akiskal et al., 1977) that observed behavioural excesses to be given precedence to mood swings in the diagnosis of cyclothymic disorder. This has also been the approach taken in the Zurich study in Switzerland (Angst, 1992). Finally the threshold of three or four out of seven signs and symptoms required for a diagnosis has yet to be validated.

It is very difficult to assess hypomania in the general population and in depressed patients who are unaware of their mood changes (Akiskal, 2002). Unlike most depressives, hypomanic subjects seldom complain of or suffer from their shifts in energy, activity and sleep behaviour but tend to experience them as positive. It is well known that such changes are more likely first to be picked up and recognised by family and friends. Thus, to focus in community studies—in the absence of collateral information from significant others — on mood changes as a gate to further probing may result in a very large number of false negative diagnoses.

It was these considerations that led us earlier to recommend (Angst, 1992) using a number of signs and symptoms of overactivity to probe for hypomania, and making relevant social consequences observed by others as obligatory criteria for the proper diagnosis of hypomania. On the basis of further analyses, we suggested removing episode-length as a diagnostic criterion. The proper definition of hypomania has important implications: it is decisive for diagnosing bipolar II disorder and subsyndromal bipolar disorder, which was found by Lewinsohn et al. (1995) to have considerable clinical validity and a prevalence rate of 5% in adolescents.

This paper will: (1) test several aspects of the diagnostic criteria of DSM-IV hypomania; (2) compare new, 'hard' and 'soft' definitions of bipolar-II (BP-II) disorder, minor bipolar disorder (MinBP) and hypomania; and (3) demonstrate the clinical validity and comorbidity of these disorders on the basis of new data from our prospective community cohort study.

2. Methodology

2.1. The definition of hypomania in DSM-IV

The DSM-IV criteria for hypomania require: (A) a distinct period of at least 4 days of elevated, expansive or irritable mood; (B) the presence of three or more of seven diagnostic symptoms (four symptoms if the mood is only irritable); (C) an unequivocal change in functioning; (D) this change and disturbance is observable by others; (E) the episode does not meet criteria for mania; (F) the symptoms are not due to the effects of a substance or a general medical condition.

The Zurich study interview for the assessment of hypomania is partly reproduced in Appendix A. Unlike other interviews, which focus on mood changes, the Zurich study stem question homes in on manifestations of overactivity: increased energy, activity, travelling, talking, being busier, feeling less tired and needing less sleep.

The second question is whether those symptoms have led to at least one of the following consequences: (1) problems for the subject himself, problems with others or financial difficulties; or (2) others in the subject's environment noticed a change in behaviour and concluded that something must be wrong with him/her: 'hypomania with conse-

quences' thus includes any hypomanic symptoms irrespective of their length and frequency.

In order to qualify for a strict Zurich diagnosis of hypomania, subjects had to have: (1) euphoria, irritability or overactivity; (2) have themselves experienced problems or received comments from others that something must be wrong with them (consequences); (3) present at least three out of seven signs and symptoms of DSM-IV hypomania.

Subjects 'with hypomanic symptoms only' (i.e., without consequences) were not excluded from this study but kept as a special soft category for further analyses. This approach is designed to avoid the loss of potential cases. 17 hypomanic signs and symptoms were assessed in 1986, and 19 (listed in Appendix A) in 1988, 1993 and 1999. Episode length was assessed but, after testing its validity, was not taken into account for the diagnosis.

2.2. The Bipolar Spectrum

The following bipolar spectrum, extended much beyond the boundaries proposed by Akiskal and co-workers (Akiskal, 1983, 1996; Akiskal and Mallya, 1987; Akiskal and Pinto, 1999), was conceptualized in an epidemiologic context, and tested for its clinical validity:

- Bipolar I disorder (MD): hospitalised mania plus major depression.
- Bipolar II disorder (Dm): DSM-III-R major depressive episodes associated with (a) a hypomanic syndrome as defined above, or (b) hypomanic symptoms only.
- Minor bipolar disorder (MinBP = md): dysthymia, minor depression or recurrent brief depression associated with (a) the hypomanic syndrome or (b) hypomanic symptoms only.
- Pure hypomania(m): (a) a hypomanic syndrome without any diagnosis of depression, and (b) hypomanic symptoms only (msx).
- Comparison group: subjects without a diagnosis of depression or hypomanic symptoms

No subjects with non-hospitalised mania were identified: in subjects meeting the criterion of a minimum episode duration of 1 week, we did not find the marked work and social impairment required for a diagnosis (assessed from the second to the sixth interviews).

2.3. Sample

The Zurich study comprises a cohort of 4547 subjects (2201 males, 2346 females) representative of the canton of Zurich in Switzerland, who were screened in 1978 with the Symptom Checklist 90-R (Derogatis, 1977). In order to increase the probability of the development of psychiatric syndromes, a sub-sample of 591 subjects (292 males, 299 females) was selected for interview, with two-thirds consisting of high scorers (defined by the 85th percentile or more of the SCL-90) and a random sample of those with scores below the 85th percentile. The screening took place in 1978 when the male probands were 19 and the females 20 years of age. So far six interview waves have been conducted as follows: (1) 1979 (M 20 years/F 21 years); (2) 1981 M 22 years/F 23 years); (3) 1986 (M 27 years/F 28 years); (4) 1988 (M 29 years/F 30 years); (5) 1993 (M 34 years/F 35 years); and (6) 1999 (M 40 years/F 41 years). Hypomania/mania were assessed from the second interview (M 22 years/F 23 years) to the sixth interview (M 40 years/F 41 years). Significant parts of the interview are reproduced in Appendix A.

A family history for each first-degree relative was obtained from the probands at the end of the interview sections for both mania and depression. Information on the sex and year of birth of each such relative was taken and, via the stem questions (see Appendix A), it was possible to assess whether or not the syndrome was present and had been treated. However no formal diagnosis of mania or hypomania among relatives was made.

At the fourth, fifth and sixth interviews (when probands were 29/30, 34/35 and 40/41 years of age), we assessed the total number of days they had spent in depression and hypomania and the frequency of depressive and hypomanic manifestations over the previous 12 months. On the basis of those data we defined rapid mood changes by the presence of four or more manifestations during 1 year; no distinction was made between major and minor manifestations. These rapid mood changes were

assessed separately for depressive and manic manifestations at all interviews. A separate, direct question (see Appendix A) was used to assess a personality with frequent ups and downs.

Probands described their overall course of their mood by referring to mood pattern graphs (not published); these were presented at the fifth and sixth interviews (M 34 years/F 35 years and M 40 years/F 41 years).

Other psychiatric diagnoses were made by algorithms according to the following criteria: anxiety states, DSM III; depression and bulimia: DSM-III-R; phobias, substance abuse/dependence, DSM-IV; neurasthenia, recurrent brief depression, ICD-10. A Zurich diagnosis of minor depression required three to four of nine DSM-III-R criterial symptoms, with a minimum duration of 2 weeks. In this study the group of mild depression consists of dysthymia, minor depression and recurrent brief depression. Subjects with one to two depressive symptoms were not classified as cases.

Conduct problems in childhood/adolescence were assessed at the age of M 27 years/F 28 years and defined as follows: (a) frequent physical fights, repeated running away, truancy, disciplinary problems at school associated with (b) psychological or psychiatric examination/treatment, severe conflicts with parents or problems with the police.

Criminal and other offenses were assessed at all interviews, and subdivided into minor offences and more serious offences (i.e., involving a court sentence).

2.4. Statistics

SAS for Windows version 8.01 was used. For group comparisons χ^2-tests, Fisher's exact tests and Kruskal–Wallis tests were applied. Prevalence rates and standard errors were computed by Stata 7.0 with adjustment for sample stratification. Cumulative prevalence rates refer to the sum of 1-year prevalence rates across all interviews. As a consequence of multiple testing, a two-tailed $P < 0.003$ was considered to be significant (Bonferroni correction).

3. Results

3.1. Validity of some diagnostic criteria of DSM-IV hypomania

We analysed the following as validators for the diagnostic criteria of hypomania: positive family history rates for mania/hypomania and depression; age of onset for hypomanic or depressive symptoms; total number of days spent in hypomania, depression and in both over the previous 12 months; diagnosis of depression; treatment of depression; suicide at-

Table 1
Validity of episode length of hypomania Impairment and number of symptoms not considered

	0 Controls ($n = 185$)	1 Hypom. 1–3 days ($n = 48$)	2 Hypom. 4 + days ($n = 95$)	3 MDD ($n = 101$)	1–2 df = 1 P	1–3 df = 2 P
No. of criterial symptoms means (s)		4.0 (2.2)	4.4 (1.5)		0.82	–
Age of onset (median)		14	14	15	0.93	0.61
FH + mania	4.2	8.7	16.5	3.5	0.22	0.02
FH + depression	30.0	50.0	48.9	64.6	0.91	0.07
Diagnosis of depression		77.1	72.6		0.57	–
Treatment of depression	14.0	60.4	47.4	58.0	0.15	0.22
Suicide attempts	2.2	16.7	8.4	23.8	0.14	0.02
Conduct problems	20.2	39.1	27.2	22.1	0.16	0.12
Offending	6.0	29.2	16.8	22.8	0.09	0.26
Hypomanic (days/1 year)	–	31.6	59.3	–	0.002	–
Depressive (days/1 year)	–	73.0	68.9	108.4	0.37	0.0001
Depr/hypom (days/1 year)		86.9	102.5	108.4	0.16	0.34

Table 2
Validity of mood plus overactivity symptoms versus overactivity symptoms: impairment, duration and number of symptoms not considered

	1 Mood symptoms + Overactivity	2 Overactivity	3 Others	1 vs. 2
Subjects	85	62	185	
Criterial manic symptoms				
Means (s)*	3.5 (1.6)	3.9 (2.1)	–	0.06
Age of onset, years (M)	14	13		0.60
Family history of mania	17.9	10.0	4.2	0.19
Family history of depres.	54.1	50.0	30.0	0.63
Diagnosis of depression	71.7	72.6	30.0	0.92
Treatment of depression	56.5	45.2	14.0	0.18
Suicide attempts	14.1	8.1	2.2	0.26
Conduct problems	28.6	31.2	20.0	0.74
Offending	25.9	16.1	6.0	0.16
Hypomanic (days/1 year)	5.7	52.0	–	0.36
Depressive (days/1 year)	73	58.7	–	0.56
Depr/hypom. (days/1 year)	94.1	94.6	–	0.45

*Five criterial symptoms of hypomania without mood items.

tempts; lifetime comorbidity with anxiety disorders, substance and alcohol abuse/dependence; conduct problems in childhood/adolescence, and offending in adulthood.

Tables 1 and 2 include all available subjects, irrespective of episode length or number of criterial signs and symptoms.

Table 1 compares subjects manifesting brief hypomanic symptoms (1–3 days) with those meeting the DSM-IV criterion of 4 days or more and also with those suffering from major depressive disorder (MDD). As expected from the definitional procedures, subjects potentially qualifying for a diagnosis of hypomania (episode of at least 4 days' duration) had spent significantly more time in hypomania in the course of the previous 12 months than had subjects manifesting brief episodes (median 40 vs. 25 days), but not in depression (median 30 vs. 30 days). All other statistical comparisons between the two groups were non-significant, and there is no systematic trend in the validators used to indicate that the longer-lasting hypomanic episodes were more severe. A positive family history for mania was slightly, but not significantly, higher among subjects whose hypomanic symptoms lasted 4 days or more.

Table 2 presents the results of a similar comparison between subjects who met the DSM-IV stem criterion A (mood changes, euphoria and irritability) plus overactivity and subjects manifesting overactivity only; the minimum length of an episode was 1 day. No difference was found in respect of any of the validators, and especially not those referring to depression. Moreover, total morbidity in terms of median days over the previous year was the same for depression, hypomania and both together. Lastly, it is noteworthy that conduct problems in childhood/adolescence were found to an equal degree in both groups; for further analyses we therefore combined the two groups, because they were associated with depression to an equal extent.

Table 3 analyses the validity of the total number of criterial signs and symptoms of DSM-IV hypomania; all subjects with criterial signs and symptoms assessed from the third to the sixth interviews (M 27 years/F 28 years to M 40 years/F 41 years) were used for this analysis. In order to have sufficient cell sizes we compared subjects with two or three symptoms ($n = 27$) with those having four or five ($n = 91$) and six or seven symptoms ($n = 29$). The group with six or seven hypomanic symptoms had spent significantly more days in depression over the previous 12 months than members of the other two groups. Otherwise no marked differences were found, and, importantly, no significant differences were found between the first and the second groups, i.e., below and above the diagnostic threshold. We concede that the small N of subjects in the first and third groups somewhat reduced the statistical power.

Table 3
Validity of number of symptoms: impairment and duration not considered

	2–3 symptoms ($n = 27$)	4–5 symptoms ($n = 91$)	6–7 symptoms ($n = 29$)	df = 2 P
Age of onset (median)	14	13	14	0.62
FH + mania %	11.1	15.7	14.3	0.84
FH + depression %	44.4	56.2	48.3	0.50
Diagnosis of depression %	66.7	70.3	82.8	0.34
Treatment of depression %	55.6	48.4	58.6	0.57
Suicide attempts %	11.1	9.9	17.2	0.56
Offending %	14.8	20.9	31.0	0.33
Hypomanic days/1 year (mean)	46.3	52.3	38.8	0.68
Depressive days/1year (mean)	48.9	51.6	115.6	0.009
Depr/hypom. days/1year (mean)	89.7	85.5	124.8	0.06

3.2. Validity of a hypomanic syndrome (Zurich criteria) versus hypomanic symptoms

The foregoing analyses led us to new questions: As the validity of the DSM-IV mood criteria tested were found to be limited, we next widened the hard definition of hypomania first to include the Zurich criteria (including overactivity, three of seven signs and symptoms, brief episodes of 1–3 days, and consequences) and compared its validity to the soft definition (symptoms only).

3.2.1. Bipolar-II disorders versus major depressive disorder (MDD)

Forty-five cases of BP-II disorder manifesting MDE plus a hypomanic syndrome with consequences (hard) were compared with 44 such cases manifesting MDE plus hypomanic symptoms without consequences (soft) and with 101 cases of pure major depressive disorder (MDD) with no manic symptoms.

Table 4 shows that the two BP-II sub-groups did not differ from each other with respect to any of the validators except for the number of criterial signs and symptoms of mania (a consequence of the group selection), whereas they did differ from MDD cases in their significantly higher rates for a positive family history for mania, comorbidity for substance and alcohol abuse/dependence, and conduct problems in childhood/adolescence. This finding is surprising and seriously questions the validity of the Zurich distinction, for our hard-soft BP-II definitions. For further analyses we therefore decided to combine the two BP-II groups.

3.2.2. Minor bipolar disorders (MinBP)

MinBP was defined by the presence of mild depression (dysthymia, minor depression, or recurrent brief depression) plus a hypomanic syndrome with consequences. The 22 cases in this group were compared with 37 cases who manifested mild depression plus hypomanic symptoms without consequences.

Table 5 shows that there was no difference between the two groups in respect of any of the validators. Because of the relatively small sample sizes, there is a risk of a type II error, but the results do not show a trend in favour of the hard definition of MinBP. The two groups were therefore combined for further analyses.

3.2.3. Hypomania

Twenty-four cases met strict Zurich criteria for pure hypomania and a further 44 cases manifested hypomanic symptoms only without qualifying for a diagnosis of any form of depression. As Table 6 shows, the two groups differed as regards comorbidity with substance abuse/dependence, which was 2-fold higher in hypomanics than in subjects with symptoms only. Although not statistically significant, there was also some difference as regards family history for mania, and the rates for offenses. Compared to the 185 controls (4.2%), a positive family history of mania was more frequent (19%) in the pure hypomanics, whose rates of substance abuse/

Table 4
Validity of hard and soft definitions of bipolar-II disorders

Diagnoses	1 BP-II hard ($n = 45$)	2 BP-II soft ($n = 44$)	3 MDD ($n = 101$)	P 1 vs. 2	P (1 + 2) vs. 3
Criterial symptoms depr. means (s)	7.6 (1.2)	7.5 (1.2)	7.4 (1.3)	0.93	0.49
Criterial symptoms man. depr. means (s)	4.2 (2.3) Median	2.9 (2.2) Median	– Median	0.002	–
Hypomanic (days/1 year)	30	50	0	0.13	n.c.
Depressive (days/1 year)	95	50	60	0.23	0.39
Dep/hypom. (days/1 year)	120	80	60	0.25	0.16
Age of onset of manic or depr. sympt. (median)	12	13	15	0.17	0.07
– of depressive symptom	14	14.5	15	0.85	0.68
	%	%	%		
Atypical syndrome	59.1	61.4	47.8	0.83	0.10
– weighted	65.9	35.9	27.0		
Course of depression					
– recurrent	68.6	63.2	65.8		
– chronic	20.0	16.7	27.9	0.63	0.43
Family history of mania	12	18	3.5	0.40	0.01
Family history of depres.	60	59	65	0.94	0.49
Suicide attempts	29	27	24	0.87	0.50
Trmt for depression	78	61	57	0.10	0.10
Comorbidity					
Anxiety disorders	71	57	54	0.17	0.18
Subst.abuse/depend.	60	50	29	0.35	0.0002
Alcohol abuse/depend.	51	39	19	0.24	0.0001
Conduct problems	44	34	22	0.34	0.02
Offenses	33	23	23	0.27	0.40

dependence and offenses were also significantly higher.

On the whole, the subjects with hypomanic symptoms had scores between hypomanics and controls; In order to be on the safe side, we did not consider subjects with 'hypomanic symptoms only' as hypomanic cases.

3.3. Prevalence rates of the hypomanic spectrum

Table 7 presents the frequencies and weighted prevalence rates of the three subgroups, BP-II, MinBP and hypomania, broken down according to the hard diagnostic threshold (hypomania with consequences) versus the soft definition (hypomanic symptoms without consequences). Of the subjects, 5.3% met the hard criteria for BP-II disorders and another 5.7% the soft symptom criterion; this combined prevalence rate of 11% for BP-II disorder was approximately the same as that for the pure major depressive disorders (11.4%).

Among subjects with minor bipolar disorder, we found higher rates on the symptom level (prevalence 6.2%) than on the diagnostic level (3.2%). A further 3.3% of the population qualified for a diagnosis of pure hypomania. As mentioned above, subjects with hypomanic symptoms only (8.9%) were not classified as cases, but were also kept separate from the controls without mood disorders.

Taking all bipolar and hypomanic cases together, we found a prevalence rate of 23.7% for the bipolar spectrum below mania; in addition we identified a prevalence rate of 0.55% for BP-I disorder ($n = 4$). The total prevalence of the bipolar spectrum including mania was therefore 24.17%, which is comparable to that for the depressive spectrum including major and milder depression (24.58%).

A strict diagnosis of DSM-IV cyclothymic disor-

Table 5
Validity of minor bipolar disorders (MinBP)

Diagnoses	1 MinBP ($n = 22$)	2 MinBP subthreshold ($n = 37$)	p 1 vs. 2
Criterial symptoms of depression means (s)	7.1 (1.5)	7.1 (1.5)	0.93
Criterial symptoms of mania + depression means (s)	3.7 (2.5) Median	2.9 (2.3) Median	0.15
Hypomanic (days/1 year)	30	20	0.10
Depressive (days1 year)	25	24	0.67
Dep/hypom. (days/1 year)	63	41	0.31
Age of onset (years)	11.5	14	0.14
	%	%	
Family history of mania	10	11	0.86
Family history of depression	64	69	0.65
Suicide attempts	9	5	0.59
Trmt for depression	68	59	0.50
Comorbidity			
Anxiety disorders	36	46	0.48
Subst. abuse/dependence	32	32	0.97
Alcohol abuse/depend.	23	30	0.56
Conduct problems	24	27	0.79
Offending	23	11	0.22

Table 6
Validity of hypomania versus hypomanic symptoms and controls

Diagnoses	1 Hypomania ($n = 23$) Median	2 Hypomanic symptoms ($n = 45$) Median	3 Controls ($n = 185$)	*P* 1–3	*P* 1 vs. 2
Hypomanic (days/1 year)	20	50			0.11
Depressive (days/1 year)	8	10			0.70
Dep/hypom. (days/1 year)	26	39			0.38
Age of onset (years)	17	15			0.65
	%	%	%		
Family history of mania	19	7	4.2	0.11*	0.15*
Family history of depression	22	43	30.0	0.15	0.09
Suicide attempts	4	7	2.7	0.43*	0.70*
Trmt for depression	13	16	14.0	0.95	0.79
Comorbidity					
Anxiety disorders	26	20	13.0	0.17	0.56
Subst. abuse/dependence	48	22	15.1	0.0008	0.04
Alcohol abuse/dependence	26	20	11.9	0.11	0.57
Conduct problems	24	14	20	0.58	0.33*
Offending	35	16	6.0	0.0001	0.08

*Small *n*.

der (requiring measurement over 2 years) could not be obtained from our data, because the morbidity of hypomania was only assessed over the 12 months preceding the interviews. If, however, we define cyclothymia according to DSM-IV criteria as applied to adolescents, i.e., as a more chronic subcategory of

Table 7
Frequencies and prevalence rates of mood disorders

	BP-II	MinBP	Hypom	Total	Major	Mild	Total
Subjects (*n*)				BP	Depr	Depr	Depr
mn syndromes	45	22	23	90	101	85	196
mn symptoms	44	37	45	126	–	–	–
Prevalence (%)							
mn syndromes	5.3	3.2	3.3	11.8	11.4	13.2	24.6
mn symptoms	5.7	6.2	(8.9)*	11.9	–	–	–
Total prevalence (%)	11.0	9.4	3.3	23.7	11.4	13.2	24.6

mn, hypomanic; *non-cases.

MinBP with a minimum total morbidity of 50% of all days over 1 year, and include dysthymics with hypomanic symptoms, 10 of 59 MinBP cases can be identified as cyclothymics (prevalence 2.0%). Applying the same 1-year time criterion, two of the 23 pure hypomanics (prevalence 0.1%) would qualify for hyperthymia.

3.4. Validity and comorbidity of bipolar and hypomanic subgroups

On the basis of the above analyses we classified the bipolar spectrum into four subcategories: BP-I, BP-II, MinBP and hypomania. As stated earlier, subjects with hypomanic symptoms only were not considered as pathological. Each category is compared in Table 8 with MDD and mild depression. 'Other depression' ($n = 85$) is a heterogeneous group consisting of 54 cases of RBD, 22 of MinD, seven dysthymics (combined either with RBD (four) or MinD (three)) and two mixed cases of RBD and MinD.

BP-II subjects differed from MDD cases in their higher rates of a positive family history for mania (14.9 vs. 3.5%), treatment for mania, rates of substance abuse/dependence (55.1 vs. 28.7%), alcohol abuse/dependence (44.9 vs. 18.8%) and conduct problems (39.1 vs. 22.1%), but the two groups did not differ as regards the family history rates for depression, suicide attempts, treatment for depression, anxiety disorders or offending. Atypical depressive features showed a trend to greater frequency among BP-II (60.2%) than MDD (47.8%); the weighted rates were 49.5 and 29.6% ($P < 0.0001$), respectively.

Compared to BP-II subjects, those with MinBP suffered from a milder form of bipolar disorder, characterised by fewer days spent in hypomania and depression and a low suicide attempt rate. On most validators their position was intermediate between the group of BP-II disorders and controls, but in the family history rate for mania, the MinBP subjects had a score of 10.5% which was significantly higher than the MDD group (3.5%) and controls (4.2%).

Of special interest is the purely hypomanic group, whose family history rate for mania (19.1%) was high compared to controls (4.2%) and whose suicide attempt rate (4.4%) was relatively low and comparable to controls (2.7%), a finding which is remarkable because pure hypomanics had high rates of substance abuse/dependence (47.8%), including alcohol abuse/dependence (26.1%), and a high rate of offenses (34.8%) and more serious offenses (13.0%).

Another surprising finding is that the majority of mood disorder subjects reported high rates of rapid mood changes (more than four per year) when asked for the number of episodes over the last 12 months. In all diagnostic subgroups rapid depressive cycling was more common than rapid hypomanic cycling. However, despite the very high rates of rapid cycling, relatively few subjects described themselves as belonging in personality to the category of people having frequent ups and downs.

4. Discussion

This paper consists essentially of two stages; in the first we test the validity of certain key DSM-IV diagnostic criteria for hypomania, and in the second

Table 8
Validity of bipolar and hypomanic subgroups

Diagnoses	1 BP-II (n = 89)	2 Min BP (n = 59)	3 Hypo-man (n = 23)	4 Man. Sx (n = 45)	5 MDD (n = 101)	6 Other Dep (n = 85)	7 Cont (n = 185)	1–7 P
Prevalence	10.95	9.40	3.23	8.86	11.41	13.18	42.38	
% Females	58.4	59.0	33.7	49.8	67.0	63.8	42.5	
Criterial symptoms of depression means (s)	7.6 (1.2)	7.1 (1.5)	4.2 (2.7)	4.3 (2.9)	7.4 (1.3)	6.1 (1.7)	2.5 (2.4)	
Criterial symptoms of mania means (s)	3.4 (2.3)	3.2 (2.4)	3.6 (1.7)	2.4 (2.5)	–	–	–	
Age of onset (years) (median)	13	14	17	15	15	16		0.0006
Hypom. (days/1 year) (means)	38	21	20	50	–	–	–	0.0001
Depressed (days/1 year) (means)	60	25	–	–	60	30	–	0.0001
Dep/hypom. (days/1 year) (means)	93	48.5	25.5	39	60	30	12	0.0001
Course pattern of depr.	%	%	%	%	%	%	%	
Recurrent	66.2	90.2	–	73.7	60.7	80.0		
Chronic	18.5	2.4	–	15.8	27.9	10.0		0.0393
Rapid cycling	82.0	96.6	60.9	82.2	53.5	81.2	46.0	0.0001
Rapid man. cycling	55.1	54.3	30.4	40.0	–	–	–	0.0864
Rapid depr. cycling	60.7	86.4	52.2	78.4	53.5	81.2	46.0	0.0001
Frequent ups and downs	42.7	32.2	8.7	13.3	23.8	10.6	3.8	0.0001
FH + mania	14.9	10.5	19.1	7.0	3.5	3.1	4.2	0.0113
FH + depression	59.6	67.2	21.7	43.2	64.6	51.4	30.0	0.0001
Suicide attempts	28.1	6.8	4.4	6.7	23.8	9.4	2.7	0.0001
Trtmt for mania/hypomania	100.0	13.5	5.1	–	–	–	–	–
Trmt for depression	69.7	62.7	13.0	15.6	57.4	42.4	14.0	0.0001
Atypical depr. syndrome	60.2	40.7	9.5	15.6	47.8	26.0	4.3	0.0001
– weighted rates	49.5	35.1	27.3	7.5	29.6	27.9	2.1	0.0001
Comorbidity								
Anxiety disorders	64.0	42.4	26.1	20.0	54.5	47.1	13.0	0.0001
Subst. abuse/dependence	55.1	32.2	47.8	22.2	28.7	22.4	15.4	0.0001
Alcohol abuse/dependence	44.9	27.1	26.1	20.0	18.8	12.9	11.9	0.0001
Conduct problems	39.1	25.9	23.8	14.0	22.1	22.7	20.2	0.0309
Offences all	28.1	15.3	34.8	15.6	22.8	16.5	5.95	0.0001
Serious offences	7.8	5.1	13.0	4.4	9.9	7.1	1.08	0.0004

'–', excluded from the statistical comparisons.

we develop a new, broader concept based on hard and soft definitions of hypomania and bipolar disorders.

Subjects reporting overactivity but no mood changes did not significantly differ from those with mood changes (euphoria/irritability) in respect of the clinical validators. This finding strongly suggests that overactive behaviour should be added to euphoric and irritable mood as a stem criterion for hypomania. This conclusion partly confirms the findings of Akiskal et al. (1977, 2001) on the importance of overactivity and our own earlier findings (Angst, 1992). In addition our study failed to confirm the relevance of the currently applied minimum length of 4 days for hypomanic episodes; brief episodes of 1–3 days were of comparable clinical significance. This finding is in agreement with the recommendations of a 2-day limit recently made by an expert group (Cassano et al., 1992; Manning et al., 1997; Akiskal et al., 2000) and used in many clinical studies (Akiskal et al., 1979, 2000; Benazzi, 2001a–c), but our concept of hypomania goes further and includes 1-day episodes as observed in adolescents, in whom very brief rapid cycling episodes are a typical feature of bipolar illness (Lewinsohn et al., 2002, in press).

The clinical validity of our hard and soft definitions of BP-II and MinBP was mainly demonstrated by their high associations with diagnoses of depression, treatment for depression and suicide attempts, and by a positive family history for mania and depression. The data suggest that the value of the Zurich hard definition of hypomania (by number of criterial signs and symptoms and consequences) should not be overestimated. Under this diagnostic threshold, any manic symptoms were shown to be relevant because they enabled the identification of soft BP-II disorders, an additional subgroup comparable in validity to the harder definition of BP-II and clearly distinct from MDD. This is a very important finding, because it doubled the prevalence rate of BP-II disorders from 5.3 to 10.95% of the population, a rate comparable to the remaining 11.4% of pure major depressives. This is compatible with the findings of Akiskal and Mallya (1987), in a clinical sample, that bipolar spectrum conditions were as prevalent as their unipolar counterparts. It is also in agreement with Benazzi (2001a), and Benazzi and Akiskal (2003), who found 45% BP-II versus 55% MDD ($n = 525$) when the stem question related to mood, and 60% BP-II versus 40% MDD ($n = 168$) when the stem question was based on overactivity.

It also accords with the finding of Lewinsohn et al. (2002, in press) that subsyndromal bipolar disorder (BD) had a previous history of MDD in 48.5% of cases, and that it predicted MDD in 40.9% in a follow-up to young adulthood. The high prevalence rate of BP-II disorder found in our study is finally in agreement with the results of the French National EPIDEP study (Hantouche et al., 1998, Allilaire et al., 2001): a careful re-examination of 537 major depressives almost doubled the rate of BP-II disorders from 21.7 to 39.8% at the expense of MDD.

The presence of atypical depressive features is considered by Benazzi (2000) and Perugi et al. (1998) to be a significant marker of bipolar II versus major depressive disorders, a hypothesis supported by an earlier prospective study of Ebert et al. (1993) showing a progression of atypical depression to bipolar spectrum disorders. Our findings lend limited support, in the form of a statistical trend, to this hypothesis, but which was significant on the basis of weighted prevalence rates.

Bipolar II patients have been shown in clinical studies to differ from MDD patients in their higher suicide attempt rates and earlier onset of their disorders (Dunner et al., 1976). However, in contrast to the six clinical studies reviewed recently by Rihmer and Pestality (1999) which found 24% suicide attempts in BP-II patients versus 12% in MDD, our study failed to provide any clear evidence (BP-II 28.1% versus MDD 23.8%). We also could not confirm an earlier onset of BP-II compared to MDD as reported in a clinical sample (Benazzi, 2001c), although we cannot exclude methodological differences in assessing age of onset. In agreement with some clinical reports (Cassano et al., 1999, Allilaire et al., 2001), we did find relatively high chronicity of depression in BP-II compared with MDD cases (18.5 vs. 27.9%).

Conduct problems in childhood/adolescence have been described as being associated with BP (Spencer et al., 2001), but at this young age they are difficult to distinguish from hypomanic symptoms (Loeber et al., 2000). Interestingly, Winokur et al. (1993) found the history of attention-deficit hyperactivity was significantly more common in the personal and family history of adult bipolars versus unipolars. Among the BP-II group the rate of conduct problems (39.1%) was about double that of controls (20.2%), but this was not true for the other subgroups of mood disorders. An important finding was that offenses in adulthood was much more common across all subgroups of mood disorders than in controls and was highest in the pure hypomanic group.

A significant new finding was the existence of a group of minor bipolar (MinBP) cases, which met diagnostic criteria for mild depression (dysthymia, minor depression, recurrent brief depression) associated with hypomanic symptoms or hypomania. These subjects did not fulfil criteria for cyclothymic disorder, because they suffered from their symptoms cumulatively only during a median of 2 of 12 months. MinBP cases were characterised by a positive family history of mania and depression, high rates of substance abuse/dependence and offending. Such cases may often be misdiagnosed as cyclothymics without meeting the chronicity criterion for cyclothymic mood disorder.

Cyclothymia and hyperthymia defined as chronic low grade versions of MinBP and hypomania; their prevalence rates were relatively low: 2.05% for

cyclothymic disorders and 0.1% for hyperthymic disorders. Our limited number of cases did not allow further analyses.

We also identified a pure hypomanic syndrome characterised by a positive family history of mania but not of depression and strongly associated with substance abuse and offending including more serious forms of crime. Our finding of a pure hypomanic syndrome would support the concept of pure mania as originally suggested by the monograph of Neele (1949), and by the nosology of Kleist (1953) and Leonhard (1957).

Perhaps the most puzzling of our findings were the high rates of rapid mood changes in the form of brief episodes, which were present not only across all mood disorder subgroups (71–97%) but were also found as brief depressive subdiagnostic mood swings among the controls (46.6%) as a normal phenomenon. In contrast to these mood swings, frequent ups and downs as a personality trait was rare in controls (3.8%), and 10 times more frequent in subjects with BP-II or MinBP disorders. Frequent ups and downs might represent a vulnerability factor for mood disorders independent of a positive family history for affective disorders (Angst et al., in press).

As expected, BP-II, MinBP and hypomania were found to be significantly associated with anxiety disorders, substance abuse/dependence and offenses in adulthood, which is in agreement with findings of psychiatric research in children and adolescence (reviewed by Lewinsohn et al., 2002, in press; Kutcher, 2000).

5. Limitations

The obvious limitations of this study are that (1) it deals with a cohort which does not represent all age groups; and (2) several of the analysed subgroups are relatively small. 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 replicate, modify or extend the present finding of very high prevalence of bipolar spectrum conditions. Of the total of 24% identified in the present study, from a public health perspective, 11% can be considered as disorder and 13% to be between disorder and normality.

6. Conclusion

We found in line with the clinical studies and conceptualization of Akiskal (1983, 2002), Perugi et al. (1998), Benazzi and Akiskal (2003), and Lewinsohn et al. (2002, in press), strong evidence for the existence of a wide and highly prevalent spectrum of bipolar syndromes and hypomania in the general population, which is clinically relevant, and in many cases only treated for depression, and which is not identifiable by the current criteria of diagnostic manuals. This paper is a further step in the recognition of the soft phenotypes of bipolar disorders even beyond those proposed originally by Akiskal and Mallya (1987), and should help to reduce pseudo-unipolar depressions. The findings overall support the broadening of the boundaries of manic depressive illness (Goodwin and Jamison, 1990) to include even the softest expression of bipolarity.

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Appendix A. Interview Section 21: Hypomania (1999)

Stem question:

Over the last 12 months and, without any special reason, have you

- been much more energetic
- been more active
- been less easily tired
- needed less sleep
- been more talkative
- travelled around more
- been busier etc.? yes no NA

Was this so evident that you had problems with it yourself, it caused you problems with others or it got you into financial difficulties? yes no NA

Did other people (e.g., family members, partner, etc.) notice these states in you and come to the conclusion that something must be wrong with you? yes no NA

Would you say you were one of those people who have frequent ups and downs? yes no NA

→If 4 times 'no', go to HISTORY

→If only 'frequent ups and downs', but no hypomania, in the last 12 months, go to HISTORY

Symptoms of the hypomania check list (HCL)

Could you describe more precisely how you experienced this? (please check all items)

(1) less sleep
(2) more strength and energy
(3) more self-confidence
(4) more enthusiasm for work
(5) more social activities (more phone calls, more visits)
(6) more travel, more (careless) driving
(7) overspending
(8) risky business activities
(9) more physical activity (moving about more)
(10) more plans and ideas
(11) less shy, less inhibited
(12) more talkative than usual
(13) thinking faster, more sudden ideas, puns and jokes
(14) easily distractible (jumping from topic to topic)
(15) more irritable and impatient higher consumption of
(16) coffee, cigarettes
(17) alcohol
(18) euphoric, overoptimistic
(19) more sexual interest other: . . . .
(20) other: . . . .

How often did such changes (episodes) occur in the last 12 months?

- once
- 2 or 3 times
- 4 to 6 times
- 8 to 11 times
- once or twice a month
- once a week
- almost every day

What was the longest period that you experienced such changes/problems ?

- 1 to 3 days
- 4 to 6 days
- 1 week or more
- 2 weeks or more
- 1 month or more
- 3 months or more

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