

## **Classification of mood disorders**

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### **Summary**

This paper looks at some recent developments in the official diagnostic definitions (DSM-5) and in the research domain. The spectrum concept of mood disorders consists of the components of depression and mania, alone or in combination, on a continuum. Its international operational classification changes regularly, being based on symptoms, their duration and consequences. Causation is as yet unknown.

DSM-5 excludes unipolar mania and mania with mild depression as separate diagnoses (they come under bipolar I and bipolar II disorders) and introduces a new hierarchy of manic symptoms, placing energy/activity above mood (elated, irritable). This is shown to be problematic on the basis of recent data. The validity of the duration criteria for mania (1 week), hypomania (4 days) and depression (2 weeks) is also seriously questioned. Shorter episodes are clinically very relevant.

The definition of mania/hypomania is a persistent problem, contributing to frequent underdiagnosis of bipolar disorder in depressed patients. Other contributory factors include that patients often do not feel ill or seek treatment for the consequences of their high mood, and that hypomania can be hidden by substance use disorders (SUD). Hidden hypomanic syndromes are important because associated with treatment resistance, high comorbidity with anxiety/panic and SUD, psychotic and cognitive symptoms, dementia and higher mortality. Anxiety, too, is doubtless a mood disorder but there is still no concept which integrates anxiety with bipolar disorder and depression. Classification involves the definition of artificial subgroups and is necessary for treatment and communication but clinicians, when in doubt, need to exercise their own diagnostic judgment especially on the basis of indicators of bipolarity in patients presenting with depression.

**Key words:** classification, depression, mania, bipolar disorder

## Introduction

The classification of mood disorders is changing constantly; this is recognised by the Diagnostic and Statistical Manual of Mental Disorders DSM-5 (2013) [1], which, in addition to the traditional categorical approach, welcomes ways of introducing more dimensional approaches – “including dimensions that cut across current categories” (p.5). Distinct categories are nonetheless necessary for communication and for treatment decisions in clinical practice. This paper will give an overview of some recent developments in the field which demonstrate the permanent state of categorical flux; it may therefore raise more questions than it can provide answers.

Figure 1 (on p. 669) presents a spectrum model of mood syndromes integrating three dimensions: 1) severity – from mood symptoms in normal subjects, via sub-threshold minor to threshold major and finally psychotic syndromes, 2) a qualitative syndromal spectrum – from depression via bipolar subgroups to mania and 3) personality/temperament traits and disorders associated with the syndromal spectrum.

### DSM-5 mood disorders: progress and problems

The most recent definitions of mood disorders are given in the DSM-5 [1], which represents an important step forward, in that it no longer excludes “antidepressant-induced” mania/hypomania as a criterion for bipolar-II/I disorder. Furthermore, it adds increased energy/activity to the two mood symptoms of the earlier editions, elated/euphoric mood and irritability, as a gate criterion A. However, DSM-5 has introduced a new hierarchy of symptoms: whereas hitherto one of the two mood items was necessary for a diagnosis, these now only count if combined with increased energy/activity.

The consequences of this change are serious, as reported recently on the basis of the data from the BRIDGE (Bipolar Disorders: Improving Diagnosis, Guidance and Education) Study [2], an international investigation comprising 5,635 patients from 18 countries seeking treatment for DSM-IV major unipolar or bipolar depression. The new DSM-5 criteria reclassified 84 (12.26%) of 685 patients with DSM-IV bipolar-I disorders as having Major Depressive Disorders (MDD), and 170 (78%) of 218 patients with BP-II disorders as having MDD. This was the direct result of the problematic new hierarchical dominance of increased energy/activity. Nonetheless, overall many more cases of MDE (Major Depressive Episode) were diagnosed as bipolar disorders: 1,513 (32%) of patients with DSM-IV MDD were classified by DSM-5 as having BP-I (N = 734) or BP-II (N = 779); this shift in diagnosis was partly due to the acceptance of switches under antidepressants and to a lesser extent to the inclusion of energy/activity as a necessary symptom. These results are remarkable: application of the DSM-5 criteria reduced the large dominance of MDD in relation to BP in our BRIDGE sample from 84% (DSM-IV) to 57.1%. We will need other and mainly epidemiological studies in order to ascertain whether bipolar disorders are as common as depressive disorders, as has been suggested by the Zurich Study [3].

DSM-5 still excludes from a bipolar diagnosis manic/hypomanic episodes occurring under substances other than antidepressants or having other causes; the data from

the BRIDGE Study suggest that this exclusion, too, may well be unjustified. Patients switching under these circumstances show strong characteristics of bipolarity (family history, age of onset, course, seasonality and resistance to treatment of depression). Treatment resistance can be an indicator of bipolarity as shown by Rybakowski [4].

It is well established that DSM-IV MDD has been over – and bipolar-II disorders underdiagnosed [5] on account of the difficulty in identifying hypomania. DSM-5 accepts hospitalisation for mania as a clear indicator for a diagnosis, while not including ambulatory treatment as an indicator for hypomania, which is inconsistent and is not validated by data. Finally DSM-5 subsumes mania under bipolar disorder, which seems illogical and, moreover, disregards the mounting evidence for its independent existence and its persistence [6].

### Definition of hypomania and mania

A correct diagnosis of hypomania is essential: not only it is seriously underdiagnosed in depressed patients but it may also explain a poorer treatment response. A better diagnosis and appropriate treatment (mood-stabilisers in combination with antidepressants) may improve patients' quality of life [4].

How to define hypomania remains an unsolved problem, as illustrated by data from the prospective epidemiological Zurich Study (1978 to 2008) [7, 8]. We tested the validity of the duration and of consequences of hypomanic episodes as diagnostic criteria. A hypomanic syndrome was defined by the presence of 4+ of 7 diagnostic symptoms. We defined three groups of syndromes by their duration: 2 weeks–3 months, 4–13 days, and 1–3 days (Table 1) and found that no statistical difference between the three groups in any of the three validators (family history, age at onset, course).

A positive family history (FH) for mania, depression, anxiety/panic was independent of the duration of hypomanic episodes, and all FH for mania, depression and anxiety were clearly higher in subjects with a syndrome of hypomania than in those with hypomanic symptoms only or controls.

Table 1. Duration of hypomanic syndromes with 3+/7 diagnostic symptoms (1986–2008)

	2 weeks–3 months	4–13 days	1–3 days	Manic sx (1981) or history of treatment*	Depr. disorders**	Others	Groups	Groups	Groups
Group	1	2	3	4	5	6	1–6	1–5	1–3
N	53	41	59	13	224	201			
Sex							p <	p <	p <
– Men	20	21	34	5	97	115			
– Women	33	20	25	8	127	86	0.02	0.20	0.11
Family history									
	%	%	%	%	%	%			
– Mania	16.98	14.63	10.17	7.69	4.46	2.99	0.0007	0.02	0.57

*table continued on the next page*

- Depression	58.49	53.66	61.02	46.15	57.14	27.86	0.0001	0.88	0.77
- Anxiety/ panic	43.40	43.90	37.29	38.46	27.23	14.43	0.0001	0.07	0.74
Age at onset									
	Mean(s)	Mean(s)	Mean(s)	Mean(s)	Mean(s)	Mean(s)			
- Mania/ hypomania	20.1 (10.07)	19.6 (8.71)	22.2 (10.69)	26.8 (10.44)	23.7 (8.61)	21.7 (6.79)	0.05	0.03	0.37
- Depression	15.6 (5.96)	16.0 (5.53)	16.6 (6.31)	14.9 (5.46)	15.6 (6.31)	16.9 (6.91)	0.64	0.79	0.60
- Anxiety/ panic	17.0 (10.65)	15.9 (8.51)	14.6 (8.38)	15.1 (9.04)	17.3 (10.20)	16.2 (9.98)	0.71	0.69	0.63
Course									
% years with manic sx	22.9 (19.13)	24.7 (18.76)	22.6 (12.91)	15.8 (12.98)	2.9 (9.78)	2.4 (12.70)	0.0001	0.0001	0.74
% years with depr sx	43.4 (30.03)	55.8 (26.91)	47.7 (25.84)	48.9 (23.07)	49.6 (27.32)	28.8 (27.93)	0.0001	0.24	0.09
% years with anx/ pa sx	31.3 (26.56)	25.0 (20.95)	30.8 (24.20)	25.3 (20.98)	29.2 (27.80)	17.0 (22.44)	0.0001	0.77	0.47

p: Kruskal-Wallis and Wilcoxon tests; \* In 1981 only manic symptoms associated with consequences were assessed. Treatment refers to years between interviews or in youth prior to the start of the study; \*\*Depressive disorders: unipolar and bipolar major or minor depression including dysthymia and recurrent brief depression

The consequences of hypomania are certainly important for a case definition, but their absence does not exclude a diagnosis, for the patients themselves are often unaware of the unfavourable consequences of their hypomanic behaviour. Information from others is needed but is often lacking. Table 2 illustrates the similarity between the family history of subjects with 4+ days hypomanic episodes and brief, 1–3 days episodes with consequences; the same was found for comorbidity with substance use disorders (SUD, tobacco not considered). This is even true for subjects reporting any kind of hypomanic symptoms: compared to controls without mood disorders, in all groups with symptoms of hypomania there are significant associations with SUD.

**Table 2. Brief episodes of hypomania 1981–2008: Family history and substance use disorders**

	4–13 days with consequences/ treatment	1–3 days with consequences/ treatment	Manic symptoms with consequences	Manic symptoms	Others	Groups	Groups	Groups	Groups
Group	1	2	3	4	5	1–5	1–4	1–3	1–2
						p <	p <	p <	p <
N	35	14	24	164	303				
Sex (N)									
- Men	15	11	10	74	156				
- Women	20	3	14	90	147	0.11	0.10	0.06	0.03

*table continued on the next page*

Family history									
	%	%	%	%	%				
– Mania	22.9	14.3	8.3	10.4	3.0	0.0001	0.21	0.33	0.51
– Depression	68.6	64.3	54.2	56.1	45.2	0.03	0.53	0.53	0.78
– Anxiety/panic	45.3	42.9	33.3	36.0	21.8	0.0001	0.22	0.28	0.47
– Suicide attempts	25.7	14.3	25.0	13.4	12.5	0.15	0.21	0.68	0.39
Substance use disorders any*									
Substance use disorders any*	54.3	50.0	50.0	43.9	28.4	0.0004	0.69	0.94	0.79
– Alcohol use disorders	42.9	50.0	45.8	35.4	20.1	0.0001	0.52	0.90	0.65
– Drug abuse/dependence	22.9	7.1	12.5	12.8	9.9	0.23	0.38	0.34	0.20
– Sedatives	22.9	14.3	20.8	9.2	6.3	0.004	0.09	0.80	0.51
– Cannabis abuse	22.9	7.1	12.5	12.8	9.6	0.20	0.38	0.34	0.20
– Stimulants	14.3	7.1	4.2	5.5	3.6	0.10	0.29	0.41	0.50

\*Tobacco not included; p: Kruskal-Wallis and Wilcoxon tests

### Definition of major depression by duration of episodes

Just as questionable and arbitrary as the four days minimum duration required for a diagnosis of hypomania is the minimum two-week episode duration for depression. In our study we broke down major depressive syndromes, defined by 5+ of 9 criterial symptoms into five groups according to their duration (3 months, 1 month, 2 weeks, 4–13 days, 1–3 days). We found no differences between the groups in regard to family history, treatment rates (in the past 12 months or over lifetime), distress, work impairment, and number of criterial symptoms [9].

In addition, a more recent analysis compared 145 subjects suffering from 2-week major depressive syndromes and 60 subjects manifesting briefer episodes but meeting a new criterion of “30+ days (4 weeks) spent in depression over the past twelve months” [10]. The two duration criteria were again found to be equally valid (family history, course and treatment rates).

Unipolar mania (M), mania with mild depression (Md), and hypomania (m)

In DSM-5 unipolar mania and mania with mild depression are not separate diagnoses but come under bipolar-I and bipolar-II disorders, and ICD-11 is set to follow suit. But this approach is not based on data.

Two large epidemiological studies have found M/Md in about 1.7% of young adults and adolescents. In Munich, the Early Developmental Stages of Psychopathology

Study (EDSP) included 3,021 adolescents and young adults and followed them for 10 years. The final prevalence rates for M was 1.5% and for unipolar hypomania (m) 3.6% [11]. In the United States, the NCS-A study of 1,0321 adolescents reported a lifetime prevalence of M/Md in 1.7% and of BP-I/BP-II disorders in 2.5% of the sample.

In a recent review of the literature on mania we confirmed that unipolar mania was reported to occur more often in non-Western than in Western countries [6].

A certain genetic independence of mania from depression was also found by two studies on the transmission of mood disorders [12, 13].

### Studies on dementia and mortality

Dementia and mortality [14] are known to be elevated in patients with mood disorders. Lithium treatment has been found to protect to a certain extent against dementia in bipolar disorders [15, 16].

Across the major mood spectrum, mortality by suicide is highest in major depressive disorders (MDD), followed by BP-II, BP-I and is lowest in M/Md. For the risk of cardio-vascular mortality, that order is reversed: compared to the general population, it is three fold higher in M/Md, double in BP-II, 1.6 times higher in BP-I and 1.3 times higher in MDD. We also found that patients with major mood disorders who described themselves as anxious lived significantly longer, perhaps on account of a more cautious lifestyle [17].

### Discussion and conclusions

As we have seen, the classification of mood disorders still remains complex and problematic. Diagnostic categories are defined as artificial subgroups on dimensional continua, for instance by number of criterial symptoms, duration, degree of distress and impairment, and course (e.g. days with symptoms over 1 year or 2 years). We are obviously still far from a true dimensional approach.

Until now MDD has dominated all other mood disorders in terms of prevalence rates and economic burden. But the newer findings reported in this paper are growing evidence of a diagnostic bias in favour of MDD and an under-estimation of bipolar disorders and mania. Future research may show that MDD accounts for no more than half of major mood disorders and that there is a continuum of proportional manic and depressive syndromes across the spectrum to pure mania.

Mood disorders in the current conception comprise mania, bipolar disorder and depression. Our investigations repeatedly found a stronger association of anxiety disorders (Generalized anxiety disorder (GAD), panic) with bipolar disorders than with depression. In recurrent brief syndromes, too, recurrent brief hypomania was more closely associated with recurrent brief anxiety than with recurrent brief depression. There is a pressing need for more research into where and how we should integrate anxiety into mood disorders; anxiety is certainly also a mood state.

Given the uncertainties of today's unipolar/bipolar distinction and the hidden bipolarity in many depressive patients, clinicians, when in doubt, still need to rely

on their own diagnostic judgment based on indicators of bipolarity: family history of mania or bipolar disorder, early onset [18], high recurrence, psychotic symptoms, mixed states, rapid onset and remission of episodes, full remission between episodes, temperament (hyperthymic, cyclothymic) and treatment resistance. Room is allowed for such an approach on the part of clinicians in both DSM-5 (296.80) and ICD F31.9.

		<b>Diagnostic Mood Spectrum</b>					
		Depression		Bipolar Disorders		Mania	
<b>Severity Spectrum</b>	Major	Major psychotic mood disorders (mc-mic)	MDD D	BP-II Dm	BP-I MD	Md Md	Mania M
	↑	Major (non-psychotic) mood disorders	MDD D	BP-II Dm	BP-I MD	Md	Mania M
	↓	Minor mood disorders (sub-treshold)	Minor depr. disorders d	Minor bipolar disorders md		Hypomania m	
		Chronic	Dysthymia	Cyclothymic disorder		-	
		Episodic	Minor depression	Recurrent minor bipolar disorder			
			Recurrent brief depression RBD-O*	Recurrent brief bipolar disorder RBD-H*		Recurrent brief hypomania	
	Minor	Symptoms (normal)	dsx	mdsx		msx	
		<b>Personality</b>					
		Temperament (normal)	Depressive temperament	Cyclothymic temperament		Hyperthymic temperament	
		Affective personality disorders	Depressive personality disorder	Cycloid/Borderline personality disorder		Hyperthymic personality disorder	

Figure 1. **Three-dimensional spectrum of mood disorders (modified from Angst 2013 [19])**

\*RBD-O (recurrent brief depression only) and RBD-H (recurrent brief depression with hypomanic symptoms) [20]

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