



Validity of bipolar spectrum?

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Disclosure /conflict of interest:

- Participation in scientific conferences sponsored by some pharmaceuticals as guest or speaker (Sanofi, Novartis, AstraZeneca, Actover, Cobel)
- Bipolar disorders specially bipolar spectrum is the main conflict of interest.

History:

- Kraepelin envisaged a continuum between manic and depressive states.
- His vision, was based on clinical observation, longitudinal course, and family history.
- This concept would enlarge the territory of bipolar subtypes, up to **50%** of all mood disorders.
- Newer classification has largely been at the expense of bipolar disorders.
- Believed that major depression and dysthymia constitute 80%, of all mood disorders.

Models of bipolar disorders:

- **Dichotomous** in regard depression: in favoring the bipolar-unipolar distinction.
- In **Continuous** with depression.
- Many of psychiatrists consider this two models in the opposites.
- Many patients who began with depression ended up with mania
- There were also patients who had a cyclical course temperamentally similar to manic-depressive patients.
- In many patients, mania and depression were intermixed in the same episode.
- Finally, patients with recurrent depression often came from families with manic-depressive illness, alcoholism, or both.

**OPERATIONAL DEFINITIONS
BIPOLAR SPECTRUM :**

Akiskal:

1. BIPOLAR ½ : SCHIZOAFFECTIVE BIPOLAR TYPE
2. BIPOLAR I: FULL-BLOWN MANIA
3. BIPOLAR I½: DEPRESSION WITH PROTRACTED HYPOMANIA
4. BIPOLAR II: DEPRESSION WITH HYPOMANIA
5. BIPOLAR II½: CYCLOTHYMIC DEPRESSIONS (BPD)
6. BIPOLAR III: ANTIDEPRESSANT-ASSOCIATED HYPOMANIA
7. BIPOLAR III½: BIPOLARITY MASKE AND UNMASKED--BY STIMULANT ABUSE
8. BIPOLAR IV: HYPERTHYMIC DEPRESSION

Ghaemi and Goodwin:

- A.** At least one major depressive episode
- B.** No spontaneous hypomania or mania
- C.** Either one of the following, plus at least two items from D, below, or both of the following plus one item from D:
 - 1.** A family history of BPD in a first-degree relative
 - 2.** Antidepressant-induced mania or hypomania
- D.** If no items from C, six of the following nine must be present:
 - 1.** Hyperthymic personality
 - 2.** Recurrent major depressive episodes (>3)
 - 3.** Brief major depressive episodes (average <3 months)
 - 4.** Atypical depressive features (eg, increased sleep or appetite)
 - 5.** Psychotic major depressive episode
 - 6.** Early age at onset of major depressive episode (before age 25)
 - 7.** Postpartum depression
 - 8.** Antidepressant tolerance
 - 9.** Lack of response to >3 antidepressants

validity of bipolar spectrum :

- Not dependent to previous models.
- Is bipolar spectrum related to bipolar category?
- Is bipolar disorder a broader concept than conventional categorization?

Approaches:

- Comparing with a standard criteria: not possible
Spectrum concept attacks standard definition
- Using methodological or philosophical system

Criteria for Diagnoses:

- Symptomatology
- Functional impairment
- Observed physical characteristics, behavior
- Illness course
- Family history
- Laboratory /biological measures
- Epidemiologic data
- Treatment response

Comorbidity and family history: BP-II vs. BP-H AA

	BP-II Sp (<i>n</i> = 144)	BP-H AA (<i>n</i> = 52)	<i>P</i>
Psychiatric comorbidity	103 (72.5%)	39 (76.5%)	0.59
Family history			
Suicide attempts	24 (17.0%)	8 (15.7%)	0.83
Completed suicide	5 (3.5%)	7 (13.7%)	0.025
Hospitalisation	40 (28.4%)	17 (33.3%)	0.51
Ambulatory treatment	70 (49.6%)	22 (43.1%)	0.43
Episodic psychiatric features	40 (28.8%)	16 (32.7%)	0.61
Chronic psychiatric features	36 (25.7%)	13 (26.0%)	0.97
At least one psychiatric disorder	78 (54.9%)	31 (60.8%)	0.47
Unipolar depression	60 (42.3%)	24 (47.1%)	0.55
Bipolar disorder	20 (14.1%)	6 (11.8%)	0.68
Schizophrenic disorder	2 (1.4%)	0	–
Alcohol abuse/dependence	23 (16.2%)	7 (13.7%)	0.68

Individual hypomanic items: BP-II Sp vs. BP-HAA

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Angst's hypomania checklist	BP-II Sp (%)	BP-HAA (%)	<i>P</i>
Less sleep	73	71	NS
More energy, strength	86	86	NS
More self-confidence	82	84	NS
Enjoying work more than usual	78	80	NS
More social activities (i.e. more telephone calls, more visiting of other people)	75	75	NS
More traveling/reckless driving	45	35	NS
Spending too much money	43	31	NS
Unwise business activities	14	6	NS
Increased activities	72	73	NS
More plans and ideas	81	78	NS
Less shy, less inhibited	79	78	NS
More talkative than usual	76	71	NS
More impatient or irritable	58	59	NS
Easily distracted	60	57	NS
Increased sex drive	48	35	NS
Increased consumption: coffee, cigarettes	36	22	0.056
Increased consumption: alcohol	26	12	0.034
Overly optimistic/euphoric	62	55	NS
Increased laughter (making jokes, puns)	61	63	NS
Thinking fast/sudden ideas	65	73	NS

Validating a BP-III variant (clinical features)

	BP-II Sp (<i>n</i> =144)	BP-H AA (<i>n</i> =52)	<i>P</i>
Hospitalised	52 (36.1%)	25 (48.1%)	0.13
Suicidal risk	21 (42%)	20 (80%)	0.002
Psychotic features	2 (4%)	2 (8%)	0.03
Treatment resistance	31 (62%) 2	19 (76%)	0.2
HAM-D 17)	24.8 (65.2)	25.4 (64.5)	0.45
HAM-D 21	26.8 (65.9)	27.3 (64.9)	0.53

Family history (FH) of mood disorders:

	BP-II Sp (<i>n</i> =144)	BP-HAA (<i>n</i> =52)	U P (<i>n</i> =253)	<i>x</i>	<i>P</i>
FH of major depression	60 (42.3%)	24 (47.1%)	102 (40.3%)	0.46	ns
FH of bipolar disorder	20 (14.1%)	6 (11.8%)	7 (2.8%)	18.3	< 0.0001

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Socio-demographic characteristics and anamnestic features

	BP-II Sp (<i>n</i> = 144)	BP-H AA (<i>n</i> = 52)	<i>P</i>
Sex ratio (M/F)	40/104	12/40	0.5
Current age (years)	43.9 (±13.2)	49.9 (±12.1)	0.005
High school or more	71 (49.7%)	18 (35.3%)	0.013
Middle to high socio-economic class of family	110 (76.4%)	31 (58.8%)	0.046
Comorbid alcohol use	93 (64.6%)	24 (47.1%)	0.028
Age of onset			
First symptoms	27.6 (±13.1)	34.3 (±16.1)	0.02
Polarity of first episode			
Hypomanic	13 (9.3%)	0	
Depressive	111 (79.3%)	49 (96.1%)	
Mixed	16 (11.4%)	2 (3.9%)	–
Stressors			
With onset of illness	110 (77.5%)	45 (88.2%)	0.09
With onset of current episode	116 (81.7%)	41 (80.4%)	0.84
Number of episodes (past year)			
Hypomania (m)	1.4 (±2.0)	0.84 (±0.7)	0.045
Depressive (D)	1.3 (±0.7)	1.5 (±0.8)	0.21
Number of episodes (lifetime)			
Hypomania (m)	5.8 (±9.9)	2.2 (±2.5)	0.01
Depressive (D)	4.9 (±5.4)	5.1 (±4.6)	0.77
Suicide attempts (last year)	27 (19.0%)	13 (25.5%)	0.33
Suicide attempts (lifetime)	58 (40.8%)	24 (47.1%)	0.44
GAF score (axis V—DSM-IV)	61.9 (±13.3)	58.4 (±14.1)	0.11

Bipolar spectrum vs. strict UP in regard HCA

	<i>N</i>	HCA (total)	F1 (“sunny”)	F2 (“dark”)
Group				
BP-II	60	11.3 (4.4)	8.6 (3.1)	2.7 (1.9)
BP-II½	161	11.4 (4.3)	8.1 (3.5)	3.2 (1.8)
BP-III	28	10.5 (4.8)	8.6 (3.7)	1.9 (1.8)
BP-IV	17	7.4 (5.5)	5.8 (4.2)	1.6 (1.5)
Strict UP	161	4.1 (3.7)	3.5 (3.2)	0.7 (1.1)
Total	427	8.4 (5.4)	6.4 (4.1)	2.1 (1.9)
<i>p</i>		<i>f</i> = 69.0 <i>p</i> <0.0001*	<i>f</i> =50.0 <i>p</i> <0.0001*	<i>f</i> =54.6 <i>p</i> <0.0001**

Is *agitated depression* a type of
bipolar mixed state :

Original article

Toward a validation of a new definition of agitated depression as a bipolar mixed state (mixed depression)

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Multivariate regression of MDE with psychomotor agitation (PA) and racing/crowded thoughts (R/CT) vs. variables typically associated with bipolar disorders, and vs. bipolar II diagnosis

Variable	F	DF	P	PA: <i>t</i>	R/CT: <i>t</i>
Bipolar II diagnosis	19.1	2, 334	0.000	4.5	4.6
Age at onset first MDE, years	6.1	2, 334	0.002	-2.0	-3.0
≥5 MDEs	4.8	2, 334	0.008	2.8	-0.9
Bipolar family history	8.8	2, 334	0.000	3.5	2.8

Multivariate regression of MDE with intense psychic tension/irritability (PT/I) and psychomotor agitation (PA) vs. variables typically associated with bipolar disorders, and vs. bipolar II diagnosis

Variable	F	DF	P	PT/I: <i>t</i>	PA: <i>t</i>
Bipolar II diagnosis	20.1	2, 334	0.000	5.2	4.5
Age at onset first MDE, years	5.9	2, 334	0.002	-3.1	-2.0
≥5 MDEs	4.6	2, 334	0.010	1.7	2.8
Bipolar family history	7.2	2, 334	0.001	2.1	3.5

Multivariate regression of MDE with intense psychic tension/irritability (PT/I) and racing/crowded thoughts (R/CT) vs. variables typically associated with bipolar disorders, and vs. bipolar II diagnosis

Variable	F	DF	P	PT/I: <i>t</i>	R/CT: <i>t</i>
Bipolar II diagnosis	21.7	2, 334	0.000	5.2	4.6
Age at onset first MDE, years	8.4	2, 334	0.000	-3.1	-3.0
≥5 MDEs	2.4	2, 334	0.091	1.7	-0.9
Bipolar family history	5.3	2, 334	0.005	2.1	2.8

Multivariate regression of MDE with intense psychic tension/irritability (PT/I), psychomotor agitation (PA), and racing/crowded thoughts (R/CT) vs. variables typically associated with bipolar disorders, and vs. bipolar II diagnosis

Variable	F	DF	P	PT/I: <i>t</i>	PA: <i>t</i>	R/CT: <i>t</i>
Bipolar II diagnosis	18.0	3, 334	0.000	5.2	4.5	4.6
Age at onset first MDE, years	6.1		0.000	-3.1	-2.0	-3.0
≥5 MDEs	3.9		0.009	1.7	2.8	-0.9
Bipolar family history	6.2		0.000	2.1	3.5	2.8

Summary of main results

Multivariate regression showed that **all the combinations** of symptoms of Koukopoulos' proposed diagnostic criteria for ***mixed depression*** were *significantly and* strongly associated with nearly all the characteristic features of bipolar disorders: **younger age at onset, MDE recurrences, BP-II lifetime, and bipolar family history.**

Conclusion:

- There is no one single gold standard test for diagnosis in psychiatry.
- Unavailability of pathognomonic diagnostic tests doesn't mean no way for correct diagnosis.
- Multi dimensional approach may be a good and practical alternative.
- By using this way, bipolar spectrum seems to belong to traditional bipolar category.