

A Model to Predict Bipolarity From the First Depressive Episode



Petra Marinova, Luchezar Hranov

University Hospital of Neurology and Psychiatry "Sveti Naum",
Department of Psychiatry, Medical University – Sofia, Bulgaria



Background:

Early differentiation between unipolar and bipolar depression bears grave implications to the course, treatment, and outcome of each of the disorders. No matter how heated the ongoing discussions are, there are no clear guidelines and further research is indicated. There is no single specific differentiating sign but various symptom constellations may indicate hidden bipolarity with a different degree of probability.

Aims:

To find indices of bipolarity in patients suffering from their first depressive episode.

Methods:

A cross-sectional non-interventional study of patients in a DSM-IV major depressive episode divided in two groups: 31 patients with recurrent unipolar depression (RUD) and 44 patients with bipolar depression (BD) (BD1 n=20; BD2 n=24) was performed. Total symptom burden was of at least moderate severity (CGI-S>4). Patients fulfilling DSM-IV criteria for mixed episode were excluded from the study. After obtaining informed consent, the participants were interviewed with M.I.N.I. 6.0 [1] and BISS [2] and completed the self-evaluation STAI [3]. A comprehensive chart encompassing a multitude of demographic and course-specific parameters was designed and imbedded during the diagnostic interview. Regression statistics for inter-group differences was performed with SPSS 16.0.

Results:

Several factors were significantly different between the two groups of patients. Out of these, five measurable variables showed prognostic value in a regression model in the first depressive episode (Table 1).

ODDS = e^(-1,32+2,21.X1+2,2.X2+1,91.X3- 0,71.X4+0,91.X5)	
X1 = Age of onset before 25 years (yes or no)	(OR = 9.109)
X2 = Evening brightening (yes or no)	(OR = 8.995)
X3 = Isolated manic symptoms* (yes or no)	(OR = 6.748)
X4 = Somatic anxiety (BISS 15) (0 to 4)	(OR = 0.489)
X5 = Lack of concentration (BISS 21) (0 to 4)	(OR = 2.478)

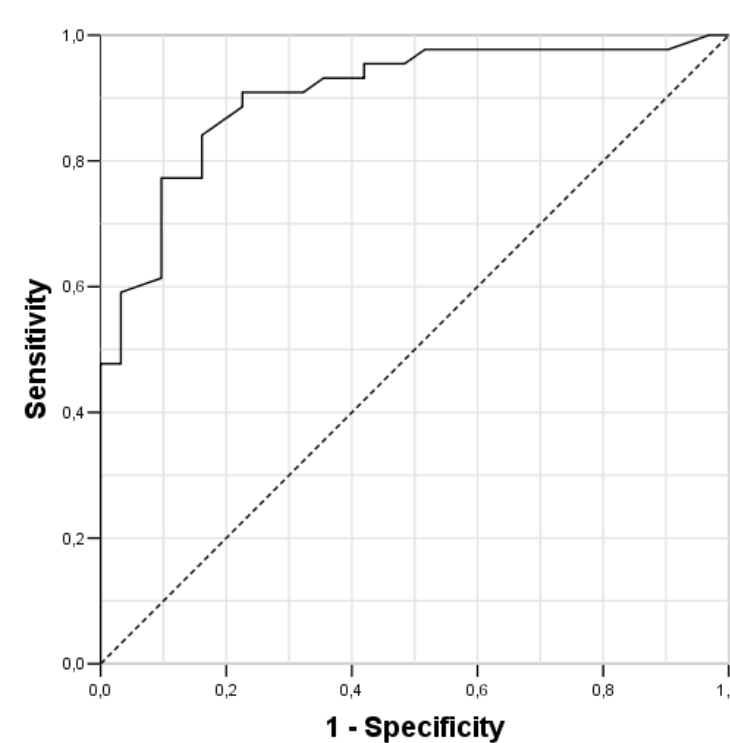
Table 1. Regression model and odds ratios (OR) of factors
*at least 1 manic item > 2 on BISS (BISS 25 to 40)

Age Onset 25 (Yes/No) =	YES
Evening Brightening (Yes/No) =	NO
BISS Manic Symptoms (Yes/No) =	YES
BISS 15 =	2
BISS 21 =	4
ODDS =	148,372951
Probability =	0,993305

Figure 1. Example screen of the program, calculating odds ratio for BD

The probability for a bipolar disorder diagnosis increased with onset of the disease before the age of 25, presence of evening brightening, isolated manic symptoms, and more severe concentration impairment within the depressive episode. Conversely, more severe somatic anxiety manifestations increased the probability of unipolar depression. The model had a high positive predictive value (PPV) of 87.8% and a negative predictive value (NPV) of 78.8%. The sensitivity and specificity were also relatively high: 83.7% and 83.9%, respectively, with AUC of 90.5%. Based on this model a program for calculating with good specificity and sensitivity the risk for bipolar disorder in a depressed patient was created (Fig.1).

Future longitudinal testing of the model would be appropriate.



AUC	SE	p	95% CI
0,905	0,035	<0,001	0,836 - 0,973

Conclusions:

There are certain signs and symptoms that can, in combination, predict hidden bipolarity during the first depressive episode with clinically acceptable sensitivity and specificity. They can reasonably well predict the future course of the disorder but the predictive value of the combined model should be tested further in larger prospective studies.

References:

- [1] Sheehan DV, Lecrubier Y, Sheehan KH, et al., 1998. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J. Clin. Psychiatry 59 (Suppl 20), 22–33.
- [2] Bowden CL, Singh V, Thompson P, et al., 2007. Development of the bipolar inventory of symptoms scale. Acta Psychiatr Scand 116:189–194.
- [3] Spielberger CD, 1983. Manual for the State-Trait Anxiety Inventory, Consulting Psychologists Press, Palo Alto, Calif, USA.

PETRA MARINOVA, MD

Currently a resident in the last fourth year of training in Psychiatry and a PhD student in Sofia, Bulgaria. Scholar of ECNP School of Neuropsychopharmacology, Oxford (2012), EPA Summer School, Strasbourg (2013), Charite's Berlin Summer School (2013). With active participation at Psychiatric meetings: 6 oral presentation during national scientific meetings and 9 poster presentations at international scientific congresses (with 7 abstracts published in international journals). Awarded with Best poster presentation at IFMAD (Barcelona, 2012) and Charite's Summer School (Berlin, 2013). Laureate of the Teodora Zaharieva Grant (Prize for medical trainees with active position) (2012/2013) and Union of Bulgarian Medical Doctors' Grant for Active Trainees (2014). Member of ECNP, Union of Bulgarian Medical Doctors, College Private Psychiatry (BG), Bulgarian Psychiatric Association, Society for Neuropsychopharmacology and Neuroscience (BG). Co-author of 3 non-peer reviewed publications in Bulgarian, 1 book chapter in Portuguese, and 2 peer-reviewed articles in English (Hranov LG., Marinova P., Stoyanova M., Pandova M., Hranov G. Bipolar disorder – from endophenotypes to treatment. *Psychiat Danub* 2013, 25 (3), 284-291; Marinova P., Koychev I., Laleva L., Kancheva L., Tsvetkov M., Bilyukov R., et al. Nightmares and suicide: predicting risk in depression. *Psychiatr Danub* 2014, 26 (2), 159-164).

Contacts: petra.marinova@gmail.com.

Background: Early differentiation between unipolar and bipolar depression is of high clinical importance for the course, treatment, and outcome of the each of the disorders. No matter how heated discussions are, there are no clear guidelines and further research is indicated. Obviously, there is no single specific differentiating sign but various symptom constellations may indicate hidden bipolarity with a different degree of probability.

Aims: To find indices of bipolarity in patients suffering from their first depressive episode.

Methods: A cross-sectional non-interventional study of patients in a major depressive episode (according to DSM-IV criteria) divided in two groups – 31 patients with recurrent unipolar depression (RUD) and 44 patients with bipolar depression (BD) (BD1 n=20, BD2 n=24). Total symptom burden was of at least moderate severity (CGI-S>4). Patients fulfilling DSM-4 criteria for mixed episode were excluded from the study. After obtaining informed consent, patients were interviewed with M.I.N.I. 6.0 [1] and BISS [2] and completed the self-evaluation STAI [3]. A comprehensive chart encompassing a multitude of demographic and course-specific parameters was designed and implemented during the diagnostic interview. A regression statistical analysis for inter-group differences was performed with SPSS 16.0.

Results: Several factors showed significant differences between the two groups of patients. Out of them, five variables measurable in the first depressive episode showed prognostic value in a regression model (Table 1).

Discussion: The probability for a bipolar disorder increased with onset of the disease before the age of 25, presence of evening brightening, isolated manic symptoms and more severe concentration impairment within the depressive episode. Conversely, more severe somatic anxiety manifestations increased the probability of unipolar depression. The model had high positive predictive value (PPV) of 87.8% and negative predictive value (NPV) of 78.8%. The sensitivity and specificity were also relatively high: 83.7% and 83.9%, respectively, with AUC of 90.5%. Based on this model a program for calculating with certain specificity and sensitivity the risk for bipolar disorder in a depressed patient was created. Future longitudinal testing of the model would be appropriate.

Conclusions: There are certain signs and symptoms that can, in combination, predict hidden bipolarity during the first depressive episode with clinically acceptable sensitivity and specificity. They can reasonably well predict the future course of the disorder but the predictive value of the combined model should be tested further in larger prospective studies.

Table 1 (abstract P.2.d.027). Parameters and characteristics of the regression model.

ODDS = exp(−1.32+2.21·X1+2.2·X2+1.91·X3−0.71·X4+0.91·X5)		AUC	p	95%CI
X1 = Age of onset before 25 years (yes or no)	OR=9.109	0.905	<0.001	0.836–0.973
X2 = Evening brightening (yes or no)	OR=8.995			
X3 = Single manic symptoms* (yes or no)	OR=6.748		RUD predicted BD predicted	
X4 = Somatic anxiety (BISS 15) (0 to 4)	OR=0.489	RUD observed	26	5
X5 = Lack of concentration (BISS 21) (0 to 4)	OR=2.478	BD observed	7	36

*At least 1 manic item >2 on BISS (BISS 25 to 40).

1. Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., et al., 1998. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J. Clin. Psychiatry 59 (Supl 20), 22–33.

2. Bowden, C.L., Singh, V., Thompson, P., et al., 2007. Development of the bipolar inventory of symptoms scale. Acta Psychiatr Scand 116: 189–194.

3. Spielberger, C.D., 1983. Manual for the State-Trait Anxiety Inventory, Consulting Psychologists Press, Palo Alto, Calif, USA.

Citation: Eur Neuropsychopharmacol. 2014;24(Suppl 2):S429

Keywords
Bipolar disorders
Depression: clinical
Diagnoses & classification