

## PSYCHOPATHOLOGICAL CHARACTERISTICS OF BIPOLAR AND UNIPOLAR DEPRESSION - POTENTIAL INDICATORS OF BIPOLARITY

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### SUMMARY

**Background:** Establishing whether a depressive episode is part of a unipolar or bipolar disorder is essential for treatment planning. Over recent years, a growing number of publications have discussed psychopathological characteristics that might serve as indicators of bipolarity in patients with a history of depression dominated by unipolar symptoms. Our primary aim was to verify the adequacy of these indicators in contributing to a precise diagnosis in everyday clinical practice.

**Subjects and methods:** We investigated 104 patients diagnosed with major depressive episode at the time of examination. 52 patients had major depressive disorder and 52 patients had bipolar disorder. The patients were then assessed for the presence of potential bipolarity indicators: psychomotor slowing, self-view (self-blaming, feelings of worthlessness), hypersomnia, increased appetite, leaden paralysis/loss of physical energy, weight increase, interpersonal sensitivity, and early morning insomnia, using the Inventory of Depressive Symptomatology. We analysed the correlations between these indicators and the presence of unipolar or bipolar affective disorder.

**Results:** Psychomotor slowing, self-blaming/feelings of worthlessness, increased appetite, leaden paralysis/loss of physical energy, and weight increase were significantly more frequent in bipolar depression than in unipolar depression ( $p < 0.05$ ). Early morning insomnia was significantly more frequent in unipolar depression ( $p < 0.05$ ). There was no statistically significant correlation between hypersomnia or interpersonal sensitivity and either of the affective disorders.

**Conclusions:** It would be worthwhile identifying the relative importance of clinical indicators for probable BP in large-scale prospective studies. These would contribute to the better diagnostic assessment of major depressive episodes and therapeutic decision-making.

**Key words:** bipolar depression - unipolar depression - bipolar disorder - indicators of bipolarity

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### INTRODUCTION

Opinions on the psychopathological characteristics of a depressive episode in unipolar and bipolar depression (BP) have evolved over time. E. Kraepelin (1899) considered the clinical manifestations of unipolar melancholy and depression to be identical during the course of manic-depressive disorder and that the only way to distinguish between them was to observe the long-term manifestations of the disease. Most contemporary researchers are of the same opinion (Sadock & Sadock 2007, Pečeňák & Švestka 2009). However, an increasing body of clinical observations and research findings indicate that the course, symptoms, genetic characteristics, and response to treatment of unipolar and bipolar depressive episodes differ.

Observing major depressive episode (MDE) symptoms in the context of a major depressive disorder (MDD) and bipolar disorder (BP), and observing the characteristics reported in unipolar depressed patients who 'convert' to BP (i.e. who later develop manic or hypomanic symptoms and diagnose is changed to Bipolar I or Bipolar II disorder) has improved the degree to which we are able to distinguish between unipolar depression and BP (Ghaemi et al. 2008,

Mitchell et al. 2008). Bipolar depression is more frequently associated with the following than unipolar depression: positive family history of BP, depression with atypical or psychotic features, psychomotor inhibition, habitual temperament instability, start of the first depressive episode in adolescence or young adulthood, mixed depressive states (depression accompanied by hypomanic symptoms, e.g. depression accompanied by increased irritability, dynamogeny, accelerated thinking and diffuse attention), and a more frequent recurrence of depressive episodes (Akiskal et al. 1995, Benazzi 1999, Benazzi 2002a, Benazzi 2002b, Hadjipavlou et al. 2004, Bowden 2005, Mitchell et al. 2008).

Resistance of depression to antidepressant treatment, the antidepressant effect of mood stabilizers, and pharmacologically induced hypomania also point to a possible bipolar nature of the affective disorder (Goodwin 2003). The use of self-assessment questionnaires, such as the Hypomania Checklist (HCL-32) (Angst et al. 2005), Mood Disorder Questionnaire (Hirschfeld et al. 2000), and the Bipolar Spectrum Diagnostic Scale (Ghaemi et al. 2005), considerably facilitates the detection of bipolarity. Early diagnosis is essential in patients with a bipolar depressive episode because adequate treatment must be started as early as

possible. Antidepressant treatment alone is inadequate in the treatment of BP, which requires treatment with a mood stabilizer or atypical antipsychotic agent, with or without combination with an antidepressant. Because of a usually late detection of bipolar disorders, some findings suggest majority of bipolar patients have been initially treated for having recurrent depressive disorder (Filaković et al. 2011).

Failure to recognize the bipolar nature of depression and treating it with an antidepressant alone may result in rapid relapse, rapid cycling, induction of hypomania, mania or mixed states, chronification of the course, only partial remission, poor quality of life, impaired social and occupational functioning, and a higher suicide risk. Different studies suggest that approximately every fourth case of MDD – and even as much as every second case using less strict criteria – is actually of a bipolar nature, which frequently passes unrecognized, and the patient receives inadequate treatment (Bowden 2001, Angst et al. 2010, Goodwin & Sachs 2010, Rogers & Agius 2012).

Instead of the categorical diagnostic approach to BP, Mitchell et al. (2008) recommend a dimensional approach, also termed the probabilistic approach. Patients with an MDE who have never suffered a manic episode are more likely to be diagnosed with BP I depression rather than MDD if five or more of the following bipolar features are present: hypersomnia and/or increased daytime napping; hyperphagia and/or increased weight; other 'atypical' depressive symptoms such as leaden paralysis; psychomotor retardation; psychotic features and/or pathological guilt; instability of mood/manic symptoms; early onset of first depression (<25 years); multiple prior episodes of depression (>5 episodes); and a positive family history of BP (Mitchell et al. 2008).

Our primary aim was to establish whether selected psychopathological characteristics regarded as indicators of bipolarity were present in patients with MDD and BP during a current MDE and to assess the importance of these indicators in the accurate diagnosis of the affective disorder present. The secondary aim was to investigate the presence of early morning insomnia. This symptom is not normally listed among the indicators of bipolarity and relatively little information has been published on its correlation with unipolar depression or BP (Mitchell et al. 1992, Benazzi 2003, Parker et al. 2000).

## SUBJECTS AND METHODS

Patients aged 18–65, diagnosed with a current MDE according to the Diagnostic and Statistical Manual of Mental Disorders criteria, Fourth Edition – Text Revision (American Psychiatric Association 2000) and treated in the psychiatric ward of the University Hospital in Trenčín, Slovakia, were consecutively enrolled into the study. Based on the clinical examination and medical history, we classed each MDE as part of a

unipolar or bipolar affective disorder. The clinically established diagnosis was confirmed by the Mini international neuropsychiatric interview (M.I.N.I. – Slovak version 5.0.0 DSM-IV (M.I.N.I.) module A – Major depressive episode, and module D – (Hypo) Manic episode (Lecrubier et al. 1998). Exclusion criteria included a depressive episode with psychotic features, depression induced by a direct effect of substances (e.g. drugs or pharmaceuticals) or a somatic disorder, or pathological grief. Patients with MDE in the context of a schizoaffective disorder or superimposed on schizophrenia, and those with schizophreniform, delusional, or psychotic disorder NOS were also excluded. Failure of the patient to understand the reasons for the investigation and inability to cooperate (e.g. serious impairment of cognitive functions) and a qualitative disturbance of consciousness over the past month were also exclusion criteria. After each BP patient was enrolled, we examined and entered one MDD patient with a current MDE, also in accordance with the inclusion and exclusion criteria. The study was approved by the local ethics committee and all patients signed an informed consent form before enrolment.

Patients with a current MDE (N=104) were divided into two cohorts. The first cohort included patients with MDD. The second cohort included patients with bipolar disorder. We used the Inventory of Depressive Symptomatology – clinician rated standardized assessment scale (IDS-C) (Rush et al. 1996) to document the following psychopathological indicators as the indicators of bipolarity: psychomotor slowing, self-view (self-blaming, feelings of worthlessness), hypersomnia, increased appetite, leaden paralysis/loss of physical energy, weight increase within the last two weeks, and interpersonal sensitivity. We also included early morning insomnia.

Indicator scores according to IDS-C are based on values of 0 to 3. In our study, we were interested in only the presence or absence of indicators and not their severity, and we therefore divided the patients up into two groups according to score: 0=indicator not present, and 1–3=indicator present.

## Statistical Analyses

Descriptive statistics were used to assess the socio-demographic characteristics of the patients. We used Pearson's chi-squared test to analyse the correlation between the presence of bipolarity indicators and diagnosis, and Spearman's rho to calculate correlation coefficients. The correlation between psychopharmacologic treatment and diagnosis was analyzed using the t-test. The statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS Version 15).

## RESULTS

104 patients with a current MDE were enrolled into the study. The patients were aged between 19 and 64

years and were predominantly female (75%). 11 unipolar (21%) and 3 bipolar patients (6%) never had a previous MDE. The mean age was 46.0 years at the time of assessment: 44.7 years in the bipolar patients and 47.4 years in unipolar patients. Based on detailed analysis of the medical history, family data, medical documentation available to us for this study, and analysis of the course of the affective disorder, we established that 8 patients who had previously suffered affective hypomanic episodes had been referred to us with a diagnosis of MDD. These patients were reassigned to the BP group. With regard to medical

history, the first depressive episode appeared before 25 years of age in 48% of the bipolar patients, but in only 31% of the unipolar patients. Socio-demographic data and details of disease history are listed in Table 1, and no statistically significant differences in given characteristics were found.

83 (80%) patients were taking psychopharmacological agents at the time of the assessment. Statistically significantly more bipolar patients were taking antipsychotic agents (37% vs. 10%) and mood stabilizers (50% vs. 13%) than unipolar patients ( $p < 0.05$ ) (Table 2).

**Table 1.** Socio-demographic characteristics

|                                       |                   | Mood disorder |             | Total       |         |
|---------------------------------------|-------------------|---------------|-------------|-------------|---------|
|                                       |                   | MDD           | n=52        | BP          | n=52    |
| Age at the time of assessment (years) | Mean (SD)         | 47.4 (11.8)   | 44.7 (11.6) | 46.0 (11.7) |         |
| Sex                                   | Men               | n (%)         | 13 (25)     | 13 (25)     | 26 (25) |
|                                       | Women             | n (%)         | 39 (75)     | 39 (75)     | 78 (75) |
| Age of onset of first MDE (years)     | <15               | n (%)         | 1 (2)       | 0 (0)       | 1 (1)   |
|                                       | 15 – 18           | n (%)         | 3 (6)       | 8 (15)      | 11 (11) |
|                                       | 19 – 24           | n (%)         | 12 (23)     | 17 (33)     | 29 (28) |
|                                       | 25 – 40           | n (%)         | 19 (37)     | 22 (42)     | 41 (39) |
|                                       | 41 – 64           | n (%)         | 17 (33)     | 5 (10)      | 22 (21) |
| Living in Partnership                 | n (%)             | 40 (77)       | 39 (75)     | 79 (76)     |         |
| Employed full-time                    | n (%)             | 29 (56)       | 17 (33)     | 46 (44)     |         |
| Retired for medical reasons           | n (%)             | 23 (44)       | 35 (67)     | 58 (56)     |         |
| Education level completed             | Basic school      | n (%)         | 5 (10)      | 2 (4)       | 7 (7)   |
|                                       | Secondary school  | n (%)         | 28 (54)     | 43 (83)     | 71 (68) |
|                                       | University degree | n (%)         | 19 (37)     | 7 (13)      | 26 (25) |

MDD - major depressive disorder, BP – bipolar disorder, SD – standard deviation, MDE – major depressive episode

**Table 2.** Type of psychopharmacological treatment at the time of assessment

| Type of psychopharmacological treatment <sup>a</sup> | MDD   | n=52    | BP                   | n=52    | Total | n=104 |
|--|-------|---------|----------------------|---------|-------|-------|
| Antipsychotics                                       | n (%) | 5 (10)  | 19 (37) <sup>b</sup> | 24 (23) |       |       |
| Mood stabilizers                                     | n (%) | 7 (13)  | 26 (50) <sup>b</sup> | 33 (32) |       |       |
| Antidepressants                                      | n (%) | 38 (73) | 34 (65)              | 72 (69) |       |       |
| Benzodiazepines                                      | n (%) | 16 (31) | 10 (19)              | 26 (25) |       |       |
| No treatment   | n (%) | 11 (21) | 10 (19)              | 21 (20) |       |       |

<sup>a</sup> combination of two or more drug in 22 (21%) of patients; <sup>b</sup> Chi-squared test  $p < 0.05$ ; MDD – major depressive disorder; BP – bipolar disorder

**Table 3.** Frequency of bipolarity indicators

| Indicator <sup>a</sup>                              | MDD               |         | BP                |                      |
|---|-------------------|---------|-------------------|----------------------|
|   | n=52              | n (%)   | n=52              | n (%)                |
| Psychomotor slowing                                 | Indicator present | 27 (52) | Indicator present | 43 (83) <sup>b</sup> |
| Self-view (self-blaming, feelings of worthlessness) | Indicator present | 15 (29) | Indicator present | 27 (52) <sup>b</sup> |
| Increased appetite                                  | Indicator present | 5 (10)  | Indicator present | 13 (25) <sup>b</sup> |
| Lead paralysis/loss of physical energy              | Indicator present | 36 (69) | Indicator present | 45 (87) <sup>b</sup> |
| Weight increase                                     | Indicator present | 3 (6)   | Indicator present | 10 (19) <sup>b</sup> |
| Early morning insomnia                              | Indicator present | 35 (67) | Indicator present | 23 (44) <sup>b</sup> |
| Hypersomnia   | Indicator present | 9 (17)  | Indicator present | 14 (27)              |
| Interpersonal sensitivity                           | Indicator present | 34 (65) | Indicator present | 42 (81)              |

<sup>a</sup> Presence defined as a score of 1–3 on the Inventory of Depressive Symptomatology – clinician rated standardized assessment scale; <sup>b</sup> Chi-squared test  $p < 0.05$ ; MDD – major depressive disorder; BP – bipolar disorder

Table 3 shows the frequency of the bipolarity indicators in the two groups. Psychomotor slowing, self-blaming and feelings of worthlessness, increased appetite, leaden paralysis/loss of physical energy and weight increase were statistically significantly more frequent in the BP patients than in those with MDD ( $p<0.05$ ). Early morning insomnia was statistically significantly more frequent in MDD patients ( $p<0.05$ ).

Spearman's correlation coefficient for the indicator and the presence of MDD or BP was positive for psychomotor slowing ( $\rho=0.424$ ;  $p<0.01$ ), self-view ( $\rho=0.243$ ;  $p<0.05$ ), increased appetite ( $\rho=0.212$ ;  $p<0.05$ ), leaden paralysis/loss of physical energy ( $\rho=0.375$ ;  $p<0.01$ ), weight increase ( $\rho=0.214$ ;  $p<0.05$ ); There was no statistically significant correlation for early morning insomnia, hypersomnia and interpersonal sensitivity.

## DISCUSSION

Our results confirm the assumption that depressive episodes in MDD and BP have different symptoms as shown by selected indicators. We observed statistically significant differences for 6 out of 8 indicators. Amongst these, only early morning insomnia occurred more frequently in patients with MDD, whilst 5 showed a significant correlation with the diagnosis of BP.

The biggest absolute difference between our MDD and BP groups was for psychomotor slowing: 83% for BP and 52% for MDD. Similar results have been reported elsewhere for patients with BP I (Mitchell et al. 2001, Mitchell et al. 2008, Mitchell et al. 2011). In patients with BP II, a long-term, prospective observational study lasting 20 years showed a cumulative incidence of psychomotor slowing in 60.7% of patients, about twice as high as the 36.6% of MDD patients who showed this (Angst et al. 2009). In 47.3% of bipolar patients in another large-scale, long-term epidemiological study, psychomotor retardation was about twice as frequent as in patients with unipolar depression (24.5%) (Weinstock et al. 2009). The absolute frequency, however, was about half of that in our patients.

Increased appetite, weight gain, and leaden paralysis were statistically significantly more frequent in patients with BP in our study. This has also been observed by other researchers. These symptoms are also considered to be the symptoms of atypical depression (Mitchell et al. 2008). Our study, however, showed no statistically significant differences for interpersonal sensitivity and hypersomnia (other atypical symptoms of depression) between the bipolar and unipolar cohorts. The indicator interpersonal sensitivity was significantly less frequently associated with BP. We also found no statistically significant correlation between hypersomnia and BP, which does not comply with other publications that report hypersomnia as a frequent symptom of BP (Mitchell et al. 2001, Benazzi 2003, Angst et al. 2006,

Mitchell et al. 2008). In several studies, most in outpatients, increased appetite and weight increase occurred more frequently in BP II than in MDD (Angst et al. 2006, Benazzi 2003). A study in hospitalized patients with BP I and MDD showed that hypersomnia, but not weight gain and increased appetite, occurred statistically significantly more frequently in BP I (Mitchell et al. 2001). Another study showed increased appetite or weight increase, or both, in 44% of bipolar vs. 25% of unipolar patients, hypersomnia in 52% vs. 31%, and fatigue in 80% vs. 59% (Weinstock et al. 2009). Leaden paralysis/loss of physical energy occurred more frequently in BP patients than MDD patients in studies reported elsewhere (Mitchell et al. 2001, Benazzi 2003, Angst et al. 2006).

We observed that self-blaming and feelings of worthlessness were statistically significantly more frequent in BP (52%) than in our unipolar patients (29%); similar results have been reported by other research groups (Parker et al. 2000, Mitchell et al. 2001).

Whilst sleep onset insomnia and reduced sleep are considered to be indicators of unipolar depression (Mitchell et al. 2008), little has been published on early morning insomnia in this context. This was the reason we included it in our analysis. It was significantly more frequent in MDD (67%) than in BP (44%).

Pharmacotherapy may have a considerable influence on the incidence and severity of the indicators we investigated. Hypersomnia, increased appetite, weight increase and psychomotor slowing are frequent adverse effects of different psychopharmacological agents, and of atypical antipsychotic and mood-stabilizing agents in particular. The correlation between the use of psychopharmacological agents and the frequency and intensity of bipolarity indicators has only rarely been investigated (Cuellar et al. 2005). Antipsychotic and mood-stabilizing agents are more frequently administered in BP than in MDD. 80% of the patients enrolled into our study were receiving some kind of a psychopharmacological agent, and significantly more patients with BP were receiving antipsychotic and mood-stabilizing agents.

## Limitations of the study

Our study reflects the common clinical practice. Indicators of bipolarity were measured in a mix of outpatients and hospital patients with higher ratio of women. A higher number of patients would have enabled us to differentiate more precisely between unipolar and BP subtypes and the severity of the current depressive episodes. The use of psychopharmacological agents was only documented as a snapshot at the time of enrolment. More frequent use of mood-stabilizing and antipsychotic agents in the bipolar cohort may have led us to overestimate the incidence of certain bipolarity indicators in patients with BP.

## CONCLUSIONS

Our results confirm the assumption that depressive episodes in MDD and BP have different symptoms as shown by selected indicators. We observed statistically significant differences for 6 out of 8 indicators. Early and accurate differential diagnosis of depressive episodes and a precise diagnosis of depression – the core feature of BP and MDD – are essential for adequate therapy and optimizing the prognosis. Even though there are no pathognomonic characteristics that enable a clear distinction to be drawn between BP and MDD, identifying clinical indicators for probable BP would provide valuable information for the clinician in everyday practice, as has been demonstrated in this study. The relative importance of such indicators for the differential diagnosis should be determined in large-scale prospective studies, also designed to investigate conversion from the unipolar to the bipolar course.

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