High neuroticism (measured by NEO-FFI) in bipolar disorder is associated with mixed state but not with rapid cycling

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Summary

Aim. Mixed episodes (MS) and rapid cycling (RC) belong to severe and destabilizing features of the bipolar affective disorder (BD) and make serious risk factors for suicide and poor long-term prognosis. Personality may determine the course and clinical expression of mood disorders. The objective of this study was to assess the personality traits in patients with or without mixed state (MS) and with and without rapid cycling (RC).
Material and methods. 108 euthymic bipolar patients (32 with MS and 28 with RC) were assessed with the use of NEO – five-factor inventory (NEO-FFI). Ratings were correlated with the clinical data of the course of BD.
Results. Neuroticism was found to be significantly higher in patients with MS as compared to those without MS history. No difference in personality measures was revealed between patients with or without RC.
Limitations. The results are limited mainly by the relatively small sample size, and also by the lack of control group of healthy individuals. It would be good to test the conclusions in other institutions.
Conclusions. The results obtained suggest that high neuroticism in bipolar patients, measured by NEO-FFI, may be associated with a predisposition to mixed state but not to rapid cycling.

bipolar disorder / mixed state / rapid cycling / personality / neuroticism.

INTRODUCTION

Mixed state episodes (MS) and rapid cycling (RC) belong to severe and destabilizing features of the bipolar affective disorder (BD). Both MS and RC are serious risk factors of suicide, related to refractoriness to treatment and higher levels of morbidity in the short- and long-term [1, 2]. The MS refers to an affective condition in which depressive and manic symptoms are simultaneously present [3]. RC is broadly defined as the occurrence, within 1 year, of four or more episodes or shifts from one pole to another.

Research into the causes of and predictors for MS and RC has focused on various areas: in MS on temperamental and biochemical correlates [4, 5, 6, 7, 8], and in RC on thyroid dysfunction and kindling phenomena [1, 2].

The attempts have also been made to establish a link between personality (including temperamental traits) and the clinical expression and the course of BD [5, 9, 10, 11, 12, 13]. Akiskal [4] and Perugi et al. [14] suggest that the origin of MS lies in the superposition of an affective episode on a pre-existing temperament of opposite polarity. Strakowski et al. [15], by using

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the temperamental concept of Cloninger et al. [16] demonstrated that patients with MS differ from others (pure manic or euthymic) in more frequent presence of harm avoidance and novelty seeking. Brieger et al. [17] found no differences in personality as assessed by NEO-five-factor model (NEO-FFI) between patients with mixed mania and patients with pure mania. We are not aware of the studies on personality factors in RC.

The objective of the study was to assess the personality traits by means of NEO-FFI, in bipolar patients with and without MS and with and without RC.

MATERIAL AND METHODS

The group studied consisted of 108 patients (53 male, 55 female), aged 22-82, mean 51.3 years (±14.3) treated in the Affective Disorder Unit of the Institute of Psychiatry and Neurology (in Warsaw, Poland) in the years 2003 – 2005. The patients were diagnosed as bipolar affective disorder, according to ICD-10 and DSM-IV diagnostic criteria [18, 19]. The study was approved by the Ethical Committee at the Institute of Psychiatry and Neurology, Warsaw. Informed consent was obtained from all patients.

The criterion for diagnosis of mixed state was the so called broad criterion, i.e. the simultaneous occurrence of either at least 3 symptoms of depressive episode and the full manic episode, or alternatively the coexistence of full depressive episode with at least 3 symptoms of manic episode. The definition of rapid cycling was that at some point in the course of the illness, 4 or more episodes occurred within not more than 1 year. Establishing the occurrence of MS and/or RC at some point during the course of BD was based on detailed clinical interview and hospital records.

The following demographic and clinical data were collected: age, sex, the family history of mental disorder, the duration of illness, the age of onset, the type of the first episode, the type of BD, the number of past depressive, manic episodes, switches from depression to mania and mixed states, treatment by antidepressants and mood stabilizers.

The persons included in the study were asked to fill out the NEO-five-factor inventory (NEO-FFI). The procedure was performed while the patients were in clinical remission. The Big Five factors of NEO and their constituent traits can be summarized as follows: neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness. The traits are measured on a scale from 0 to 48 [20].

The data have been stored in an Excel spreadsheet [21], the WinSTAT for Excel software was used for data processing and analysis [22]. Statistical significance of observed differences between mean values was assessed by the t-test for independent pairs and for the fraction of given group by the chi square test (χ^2), with Fisher's correction for small sample size. Statistical significance was tested at the level of $p < 0.05$. Multivariate analysis (logistic regression) was also performed.

RESULTS

The MS was diagnosed in 29.6% of patients (32/108, 17 females and 15 males) and RC in 25.9% of patients (28/108, 13 females and 15 males). A significant relationship was found between the occurrence of MS and RC. Seventeen patients had both MS and RC course, which makes 53% of MS and 61% of RC ($p < 0.001$).

Demographic and clinical data of the patients are presented in Table 1.

The compared groups did not differ in age, sex, the age at onset, the duration of the disease, and the family history of mental illness. The use of antidepressants and mood stabilizers was very similar in both groups. There were differences in the previous course of the BD: in both MS and RC group there was a higher number of previous switches from depression to mania and the type I course of disease. The RC group had a higher number of manic episodes.

A comparison of personality features of the groups with and without MS and with and without RC is presented in Table 2.

Neuroticism was significantly higher in the patients with MS than in those without MS. No differences were found between patients with and without MS in the course of BD in the remaining personality features. No significant differences in personality traits were found in the patients with and without RC.

Table 1. Clinical characteristics of bipolar patients with and without MS and with and without RC

	Mixed n = 32	Non-mixed n = 76	Rapid cycling n=28	Non-rapid cyclingn=80
Gender, no, of female patients (%)	15 (46.9)	40 (52.6)	13 (46.4)	42 (52.5)
Age, years, mean (SD)	49.7 (15.3)	52.0 (14.0)	49.9 (16.1)	51.8 (13.8)
Family history of mental disorders, n (%)	12 (37.5) 5 (15.6)	24 (31.6) 10 (13.2)	9 (32.1) 3 (10.7)	27 (33.7) 12 (15)
Duration, years, mean (SD)	15.3 (10.8)	14.2 (9.0)	12.6 (7.5)	15.2 (10.1)
Age of onset, years, mean (SD)	34.5 (12.1)	37.9 (13.6)	37.3 (14.5)	36.7 (12.8)
Type of BD, n (%)				
I	23 (71.9)	25 (32.9)*	22 (78.6)	26 (32.3)#
II	9 (28.1)	51 (67.1)	6 (21.4)	54 (67.5)
No of manic episodes, mean (SD)	3.6 (3.8)	3.6 (3.5)	4.6 (3.9)	2.9 (2.0)#
No of depressive episodes, mean (SD)	6.3 (4.4)	5.9 (3.4)	6.3 (4.0)	5.4 (2.8)
No of switches from depression to mania, mean (SD)	3.7 (3.6)	1.7 (2.6)*	3.7 (3.7)	1.4 (1.4)#
Use of antidepressants, n (%)	29 (90.6)	74 (93.4)	26 (92.8)	77 (96.3)
Use of mood stabilizers, n (%)	28 (87.5)	61 (80.3)	21 (75)	68 (85)

* difference between MS and non-MS significant, p<0.05

difference between RC and non-RC significant, p<0.05

Table 2. NEO-FFI traits in patients with and without MS and in patients with and without RC

NEO-FFI trait	Mixed n = 32	Non mixed n = 76	Rapid cycling n = 28	Non rapid cycling n = 80
	mean (SD)	mean (SD)	mean (SD)	mean (SD)
Neuroticism	30.4 (9.6)	26.0 (9.5)*	27.5 (9.0)	27.4 (10)
Extraversion	24.4 (8.9)	24.7 (7.8)	22.9 (7.5)	25.0 (8.4)
Openness to Experience	26.9 (8.6)	26.3 (5.7)	27.2 (6.7)	26.3 (6.8)
Agreeableness	31.2 (6.8)	30.5 (6.0)	31.9 (5.2)	30.3 (6.7)
Conscientiousness	29.7 (10.7)	30.3 (7.7)	28.0 (9.4)	30.8 (8.3)

*Difference between MS and non-MS significant p<0.05

Multivariate analysis (logistic regression), with personality traits and some clinical factors (e.g. MS and RC) as regressors did not produce a model with statistically significant explanatory power (p in the range 0.27– 0.32).

DISCUSSION

The main finding of our study is showing an association between high neuroticism and a tendency to mixed state episodes in bipolar patients. On the other hand, no association was revealed between personality factors as measured by NEO-FFI and tendency to rapid cycling. The association of high neuroticism with MS and not with RC has been revealed despite of the fact that these two groups were partly overlapping.

Neuroticism has been a personality dimension extensively studied in affective disorders. Neuroticism correlated with higher risk of occurrence of affective disorders in general (particularly depression), while the bipolar form was rather related with extraversion [23]. Both neuroticism and predisposition to mood disorder have been associated with polymorphism of serotonin transporter gene [24]. Recently, Munafo et al. [25] suggested that neuroticism mediates the association of the serotonin transporter gene with lifetime major depression. Heerlein

et al. [9] observed a correlation of high neuroticism with a high number of recurrences, poor quality of remissions and chronicity of the disease. Clayton et al. [26] expressed the opinion, that high neuroticism and low extraversion are predictors of recurrent depressions, but not of BD. One paper using NEO-FFI is that of Brieger et al. [17], who assessed patients during mixed or pure mania episodes and found no differences between these two groups.

In our previous study, it was found that temperament trait (endurance) as defined by Strelau scale [27] may make a good predictor of the risk for both MS and RC in patients with BD [28]. MS and RC are similar in that that they both lead to severe forms of the illness and in both forms it is advisable to avoid using destabilizing medication such as antidepressants and using mood stabilizers. However, in our present study we found that higher neuroticism is characteristic of the MS patients but not for RC. This may point to possible different underlying mechanisms of these two conditions. In the case of MS, it may be a "depressive" trait, while in the pathomechanism of RC, additionally, a "switch" to mania may play a role. This was reflected in our results where the RC group had a higher number of manic episodes. On the other hand, Zarate et al. [29] found that patients with mixed presentations of bipolar illness are more likely to cycle to a depressed phase without recovery from the index episode. Also, the discrepancy of our results with those of Brieger et al. [17] may be due to the fact that these authors studied entirely mixed manic states but not mixed depressions.

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Nr 3 (146 2008

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