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Research Article

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The Big Five Model in Bipolar Disorder: A Latent Profile Analysis and its Impact on Longterm Illness Severity

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Abstract

Background: Using a personality typing approach, we investigated the relationship between personality profiles and the prediction of longterm illness severity in patients with bipolar disorder (BD). While previous research suggests associations between BD and traits from the NEO-FFI profiles, the current study firstly aimed to identify latent classes of NEO-FFI profiles, and, secondly, to examine their impact on the longterm prognosis of BD.

Methods: Based on the NEO-FFI profiles of 134 euthymic patients diagnosed with BD (64.2% female, mean age = 44.3 years), successive latent profile analyses were conducted. Subsequently, a subsample (n = 80) was examined prospectively by performing multiple regression analysis to evaluate the longitudinal course of the disease (mean: 54.7 weeks) measured using a modified Morbidity Index.

Results: The latent profile analyses suggested a 3-class model typifying in a resilient (n = 68, 51%), vulnerable (n = 55, 41%) and highly vulnerable (n = 11, 8%) class. In the regression analysis, higher vulnerability predicted a higher longterm Morbidity Index (R^2 = .28).

Conclusions: Subgroups of patients with BD share a number of discrete personality features and their illness is characterized by a similar clinical course. This knowledge is valuable in a variety of clinical contexts including early detection, intervention planning and treatment process.

Introduction

The present study uses the *Big Five* personality typology to predict the longterm course of bipolar disorder (BD), thus addressing the gap in prospective research of this recurring psychiatric disorder. There is an ongoing debate about how personality factors relate to the development, expression and prognosis of clinical disorders. Klein *et al.* (1) illustrated six models to describe the nature of the association between personality and mood disorders. The *common cause* and *precursor* models view personality as an antecedent to the disorder, where both are underpinned by the same etiological factors. In the precursor model, personality traits represent early, subclinical features of the disorder. The *predisposition* and *pathoplasticity* models depict personality as a risk factor for the onset (or severity and course, respectively) of a disorder without implying the same etiological origin. With a reverse causal direction, the *concomitant (state-dependent)* model assumes that personality assessments are influenced by the patient's current mood state. In a similar vein, the *complication (scar)* model proposes that personality is permanently altered by the disorder with no return to its baseline state.

The *Big Five* personality comprises traits of neuroticism, extraversion, openness to experience, agreeableness and conscientiousness (2) and forms the basis of several personality inventories (3). Subjects may not only be differentiated by their score on individual personality factors, but also on *profiles* composed of these factors. Thus, subgroups (or classes) of similar profiles can be identified. Latent profile analysis (4) is an extension of latent class analysis assuming unobserved (latent) categorical variables (classes) to explain similarities between continuous manifest indicators. For example, in a therapy study with major depressive disorder patients, Wardenaar *et al.* (5) extracted two latent classes based on the *NEO Five-Factor Inventory* (NEO-FFI; German version: 6): The vulnerable class was characterized by high neuroticism as well as low extraversion and conscientiousness, while the resilient class was characterized by mod-

erate neuroticism and extraversion, and high agreeableness and conscientiousness. Furthermore, the authors showed that belonging to the resilient personality class was predictive of being successfully treated more quickly.

Bipolar affective disorders are chronic psychiatric conditions characterized by recurring depressive and manic (bipolar type I) or hypomanic (bipolar type II) mood episodes, with interepisode intervals of remission or decreased symptoms (euthymia). Certain personality factors have already been linked with particular psychiatric disorders (7), however a line of research has extended on this topic by exploring personality variables as possible predictors of the clinical course of BD. For example, Lozano and Johnson (8) found that high neuroticism longitudinally predicted increasing depressive symptoms, while high conscientiousness predicted increasing manic symptoms. Further, neuroticism has been found to predict poorer sleep quality (9). Neuroticism, agreeableness, and conscientiousness affect suicidality (10), and low extraversion, openness and conscientiousness are associated with polypharmacy (11). Previous research has also indicated several other demographic and clinical variables to be related to the course of BD. These include gender, age at onset, pattern of episodes, BD subtype, rapid cycling, depressive symptoms, and co-morbid conditions (12, 13). Additionally, the development of BD from an initial unipolar depression diagnosis was associated with a higher level of extraversion (14).

In studies where the course of BD has been measured prospectively, *period until next affective episode* (time to relapse) has generally been regarded as an essential outcome measure. However, Baethge *et al.* (15) have argued for a more sophisticated approach, namely using the Morbidity Index (MI). The MI is calculated based on weekly observations of the patient's symptomatology while controlling for total observation time. By continuously collecting data, a more robust measure of the course of the illness is achieved. In addition to this concept, we introduced also subsyndromal symptoms into the calculation of the MI (16) as there is much evidence that

bipolar patients also can be differentiated by a strict euthymia criteria versus subsyndromal depressive or hypomanic symptoms.

With the present study being one of the first of its kind to examine bipolar patients' personality profiles as prospective course modifiers, the general goal of the research is to provide a basis for using a comprehensible typology in communication with clinical professionals or patients. Such a typology would be invaluable to clinicians in screening for early BD symptoms; for deriving appropriate, individually-tailored interventions; and for establishing the prognosis and probable treatment outcome. The aims of this study are therefore twofold: First, we aim to classify BD based on patients' NEO-FFI scores by applying latent profile analysis and to characterize the emerging latent classes. In a second step, we aim to predict the treatment course (indicated by the MI) using the obtained personality classes.

Method

Participants

The sample consisted of 134 patients (64.2% female, mean age = 44.3 years), 64.9% of whom had been diagnosed with bipolar I disorder while the remaining 29.9% had a bipolar II diagnosis. Further demographic features and disorder-related characteristics are listed in Table 1 (see column *Total sample*).

Participants were part of a larger, prospective multi-center study conducted between May 2004 and 2011 in three university clinics across Germany and Austria (Berlin, Dresden, and Neunkirchen). For the present analyses, subgroups that completed the NEO-FFI (6) were examined.

Participants were recruited from outpatient clinics specialized in the treatment of BD. The following primary inclusion criteria applied: Diagnosis of BD I/II according to the *Structured*

Clinical Interview for DSM-IV (SCID I/II; German version: 17), treatment with psychopharmacological drugs, mental and physical capabilities that enabled the patient to participate and establish informed written consent (e.g., fluent German language). Exclusion criteria were having a diagnosis of an organic brain disorder, having another predominant axis I disorder, and acute suicidality.

Measures

Diagnoses and psychopathology

While patients were previously diagnosed with BD, their diagnosis was verified by clinical interview using the SCID. Current psychopathological state was assessed using the *Hamilton Depression Rating Scale* (HDRS-21, 18) and the *Young Mania Rating Scale* (YMRS, 19), both of which provided observer ratings on the severity of depressive and (hypo-)manic symptoms, respectively.

Personality assessment

Participants chosen for the current analyses completed the *NEO-FFI* at baseline. This self-report instrument consists of 60 statements rated on a 5-point Likert-type scale (1 = *strongly disagree* to 5 = *strongly agree*). Its factor structure conforms to the five factor model of personality (20, for a clinical sample) and every subscale has shown adequate internal consistency and temporal stability (α = .72 to .87, r = .71 to .82, 6). Personality assessment was conducted only if patients were in stable remission.

Prospective assessment

After baseline assessment, the patients' course of illness was investigated prospectively at least every eight weeks in terms of the following variables: Current psychopathology (HDRS, YMRS), duration and polarity of relapse, change of medication, type of medication, and necessity of hospitalization. Longitudinal illness severity was measured using the MI. At each follow-up assessment, scores on the MI were updated based on the psychiatrist's current psychopathology rating; where 'degree 1' signified mild symptoms, 'degree 2' signified aggravation with a need for additional treatment, and 'degree 3' signified aggravation and an acute need for hospitalization. In order to detect minor depressive and manic symptoms, a subthreshold parameter of 0.5 was integrated using adjusted cutoff scores on symptom measures (HDRS-21 ≥ 4 and ≤ 9; YMRS ≥ 3 and ≤ 11). The resulting sum was divided by the total observation time, resulting in values ranging between zero and 1.47 ($M = 0.44$, $SD = .37$), with a high MI indicating a poorer outcome. The modified MI calculation for our sample is described in detail in Rote *et al. (16).*

Procedures

Figure 1 displays the exclusion of patients across different stages of our investigation and the resulting sample sizes for the respective analyses.

Altogether, the baseline assessment involved extensive collection of demographic and psychological variables (personality, quality of life, sleep quality), psychopathology (clinical and self-ratings of depression and [hypo-]mania), anamnestic information (patient history concerning past episodes, rapid cycling, hospitalization, suicide attempts, substance consumption) as well as past and current medication. To minimize the potential risk of assessing concomitant current mood states, the personality assessment was only proceeded providing those participants were euthymic; which was confirmed by assessment using the SCID interview and other symptom

measures (HDRS-21 ≤ 9 and YMRS ≤ 12). If euthymia criteria were not met, participants were excluded.

The follow-up sessions were scheduled every eight weeks for two years, but actual observation time varied among patients due to various reasons, e.g., illness or hospitalization (Range = 1 to 122 weeks, M = 54.7, SD = 34.9). Where assessment intervals exceeded 20 weeks, or where total observation time was less than eight weeks, participants were omitted from further analyses. This resulted in a final sample of 94 patients who provided prospective data, of whom 80 yielded valid data on the selected predictor variables and were thus used in the multiple regression analysis.

Figure 1

Fig. 1. Flowchart of the sample including reasons for the exclusion of patients. NEO-FFI (NEO Five-Factor Inventory).

Statistical analyses

Means for the five NEO-FFI subscales were calculated based on the valid items (ipsative mean imputation; 21) taking into account the low rate of missing data (0.8% of the values) and the reliability of the NEO-FFI scales. We evaluated the pattern of missing data among the demographic and clinical variables by applying Little's (22) omnibus MCAR test which indicated that data were missing due to completely random purposes; $X^2(349) = 340.57$, $p = .617$. Hence, we applied pairwise deletion of the affected cases to test for group differences.

Latent profile analysis (4) was used to group similar patients using probability based on their individual NEO-FFI profiles. For our analyses, all five NEO-FFI subscales were entered into the latent class model. We chose maximum likelihood estimation with robust standard errors, with variances held equal across classes and covariance among the latent class indicators fixed

at zero. To reduce the risk of local maxima, the initial number of random starting value sets was set at 500, and the 50 best sets (according to their likelihood values) were selected for optimization after 50 iterations (23). After conducting a series of successive latent profile analysis models with increasing numbers of latent classes, the decision regarding the number of obtained classes was empirically and conceptually driven (i.e., being mindful of the interpretability of the class solution).

To validate the latent classes, *group comparisons* were performed to test for differences at baseline. Analyses of variance (ANOVA) were performed for parametric variables. Kruskal-Wallis tests and subsequent Man-Whitney tests with Bonferroni corrections for multiple post hoc comparisons were used for non-parametric variables. Dichotomous categorical variables were analyzed using Fisher's exact test.

To assess the longitudinal treatment effect, a *hierarchical multiple regression* was conducted with the MI as the outcome variable, regressed on the dummy-coded latent classes as well as on a set of clinical variables previously found to predict the course of BD (12). Of the potential predictor variables, those with significant correlations with either the outcome or another chosen predictor were included in the regression analysis (24).

We used Mplus version 7.4 (4) to perform the latent profile analyses, and IBM SPSS Statistics version 21.0 for all further analyses.

Results

Clinical characteristics

Table 1 (column *Total Sample*) summarizes the clinical features of our sample. With an average age at onset of 27.2, our subjects had an average of 15.4 past episodes during their course of

BD and a mean of three hospitalizations. Twenty percent suffered from previous rapid cycling and 30.6% reported previous suicide attempts.

Table 1. *Sample characteristics and differences between personality classes*

Variable	Total Sample (N = 134)	Class 1: Resilient (n = 68)	Class 2: Vulnerable (n = 55)	Class 3: Highly vulnerable (n = 11)	Statistics	
					p Value	Effect Size
Bipolar I subtype (% yes)	87 (64.9)	47 (69.1)	34 (61.8)	6 (54.5)	n.s.[a]	V = .07[b]
Demographic variables						
Gender (% female)	86 (64.2)	43 (63.2)	35 (63.6)	8 (72.7)	n.s.[a]	V = .05[b]
Years of age – *M* (*SD*)	44.3 (13.3)	45.1 (13.5)	43.7 (13.5)	41.9 (10.7)	n.s.[c]	ω^2 = -.01
# Years of education – *M* (*SD*)	13.5 (3.2)	13.8 (3.1)	13.4 (3.3)	12.2 (2.8)	n.s.[d]	η^2 = .01
Employment (% yes)	69 (51.5)	34 (50.0)	30 (54.5)	5 (45.5)	n.s.[a]	V = .06[b]
Relationship Status (% in relationship)	69 (51.5)	37 (54.4)	26 (47.3)	6 (54.5)	n.s.[a]	V = .07[b]
Clinical variables						
Substance Use (% yes)						
Alcohol	39 (29.1)	21 (30.9)	15 (27.3)	3 (27.3)	n.s.[a]	V = .03[b]
Drugs	16 (11.9)	8 (11.8)	6 (10.9)	2 (18.2)	n.s.[a]	V = .06[b]
Co-morbidity[e] – *M* (*SD*)	0.31 (0.64)	0.2 (0.52)	0.29 (0.52)	1.25 (1.16)	p = .002** [d]	η^2 = .10
Medication[f] – *M* (*SD*)	1.80 (1.01)	1.78 (1.18)	1.78 (0.85)	2.1 (0.57)	n.s.[d]	η^2 = .00
Age at onset – *M* (*SD*)	27.2 (10.2)	29.3 (9.6)	24.5 (10.2)	27.3 (11.3)	p = .023* [d]	η^2 = .04
Past episodes – *M* (*SD*)	15.4 (16.2)	14.9 (17.9)	16.3 (15.5)	13.6 (10.1)	n.s.[d]	η^2 = .00
Previous rapid cycling (% yes)	27 (20.1)	11 (16.2)	14 (25.5)	2 (18.2)	n.s.[a]	V = .11[b]
# Hospitalizations – *M* (*SD*)	3.0 (3.1)	3.0 (2.6)	2.8 (3.4)	4.3 (3.8)	n.s.[d]	η^2 = .00
Attempted suicide (% yes)	41 (30.6)	19 (27.9)	20 (36.4)	2 (18.2)	n.s.[a]	V = .12[b]
NEO-FFI scales – M (SD)						
Neuroticism	1.96 (0.71)	1.44 (0.45)	2.39 (0.42)	3.10 (0.34)	p < .001*** [d]	η^2 = .67
Extraversion	1.99 (0.6)	2.25 (0.48)	1.88 (0.52)	1.0 (0.43)	p < .001*** [d]	η^2 = .27
Openness	2.43 (0.55)	2.36 (0.59)	2.54 (0.46)	2.25 (0.55)	n.s.[c]	ω^2 = .02
Agreeableness	2.53 (0.43)	2.68 (0.38)	2.45 (0.41)	2.04 (0.43)	p < .001*** [c]	ω^2 = .17
Conscientiousness	2.52 (0.55)	2.85 (0.4)	2.31 (0.41)	1.55 (0.25)	p < .001*** [c]	ω^2 = .49
Morbidity Index – *M* (*SD*)	0.44 (0.37)	0.30 (0.31)	0.53 (0.35)	0.9 (0.35)	p < .001*** [d]	η^2 = .19

Note. NEO-FFI = NEO Five-Factor Inventory

[a] Fisher's exact test, [b] Cramer's *V*, [c] F(2,131), ANOVA, [d] H(2), Kruskal-Wallis test, asymptotic significance, [e] number of co-morbid axis I or II diagnoses, [f] number of current psychotropic medication groups (lithium, anticonvulsants, neuroleptics, and antidepressants).

* p < .05, ** p < .01, *** p < .001.

Latent Profile Analysis

With regards to our primary research question, the detailed results for the increasing latent class models are displayed in Table 2. We selected the 3-class model to represent our data as it achieved the lowest BIC value which is recommended when determining the number of latent classes (25).

Table 2. *Latent class model fit indices*

Model	FP	Log-likeli-hood	Entropy	AIC	BIC	aBIC	BLRT *p* value	VLMRT *p* value
1-class	10	-561.1	-	1142.1	1171.1	1139.5	-	-
2-class	16	-525.3	0.687	1082.6	1128.9	1078.3	.000***	.020*
3-class	**22**	**-509.9**	**0.750**	**1063.7**	**1127.5**	**1057.9**	**.000*** **	**.009** **
4-class	28	-501.4	0.750	1058.7	1139.9	1051.3	.112	.337
5-class	34	-493.5	0.785	1055.0	1153.5	1046.0	.208	.509
6-class	40	-487.4	0.812	1054.9	1170.8	1044.3	.598	.394

Note. The best fit model is shown in **bold**. FP = number of free parameters, AIC = Akaike information criterion, BIC = Bayesian information criterion, aBIC = sample size-adjusted BIC, BLRT = Bootstrap Likelihood Ratio Test *p* value for (k-1) classes, VLMRT = Vuong-Lo-Mendell-Rubin Likelihood Ratio Test *p* value for (k-1) classes.

* $p < .05$, ** $p < .01$, *** $p < .001$.

Figure 2 displays the plotted NEO-FFI subscale means of the three classes based on the estimated model. The resulting classes were characterized by their low/high scores on the Big Five scales in comparison to the means of the other classes. We interpreted and labeled the classes according to Wardenaar *et al.* (5) as *resilient, vulnerable* and *highly vulnerable,* whereby:

- **Resilient** class (n = 68; or 51% of our sample) is characterized by low neuroticism, high extraversion, high agreeableness and high conscientiousness,

- **vulnerable** class (n = 55; 41%) is characterized by higher neuroticism, lower extraversion, lower agreeableness and lower conscientiousness, and
- **highly vulnerable** class (n = 11; 8%) is characterized similar to the *vulnerable* class but with even higher neuroticism, lower extraversion, lower agreeableness and lower conscientiousness.

Figure 2

Fig. 2. Class-specific personality profiles for the 3-class model. NEO-FFI, NEO Five-Factor Inventory.

Personality Class Characteristics

To validate our latent class model, we examined descriptive characteristics of the obtained three classes. Results of these secondary explorative analyses are shown in Table 1. The classes did not differ in terms of any *socio-demographic variable*. To address the question as to which clinical variables might be associated with belonging to a specific personality class, the analyses revealed the number of co-morbid diagnoses and age at onset as significant correlates. Pair-wise comparisons regarding the former indicated significantly more *co-morbid disorders* in the highly vulnerable (*Mdn* = 1.5) compared to the vulnerable (*Mdn* = 0) and resilient (*Mdn* = 0) classes ($U = 79$, $p = .010$, $r = .38$ and $U = 106$, $p < .001$, $r = .43$, respectively). The resilient and vulnerable classes did not differ in their number of co-morbid disorders ($U = 947$, $p = .188$, $r = .14$). With regard to *age at onset,* pair-wise comparisons of the obtained classes indicated a significant difference between the vulnerable and resilient classes ($U = 1280$, $p = .006$, $r = .25$) with patients in the vulnerable class having an earlier onset age (*Mdn* = 21.5) than those in the resilient class (*Mdn* = 29). Age at onset in the highly vulnerable class did not significantly differ

from the other classes (*Mdn* = 27, *U* = 321, *p* = .495, *r* = .08 and *U* = 256.5, *p* = .478, *r* = .09, respectively).

Prediction of longterm illness course

To answer our second research question regarding the influence of the personality classes we established on the illness course, we initially scanned the correlation matrix of potential predictors and the MI. Significant correlates of the MI were the number of past episodes, r_S = .24, p = .028, and assignment to the latent personality class, r_S = .44, p < .001. Furthermore, the number of past episodes was correlated with rapid cycling (lifetime), r_S = .49, p < .001, and the personality class variable correlated with age at onset, r_S = -.21, p = .040, and the number of co-morbid diagnoses, r_S = .27, p = .010. Due to parsimony of the intended regression model (24), we did not inspect further significant correlates of potential predictor variables.

Table 3 displays the results of the multiple regression analyses predicting patient MI. In a first step, we simultaneously entered the number of co-morbid diagnoses, age at onset, number of past episodes, and rapid cycling into the regression model. None of these variables significantly predicted our outcome, R^2 = .11, $F(4,75)$ = 2.28, p = .069. In a second step, we added the dummy-coded personality classes. This resulted in a significant improvement predicting the MI, R^2 = .28, ΔR^2 = .17, $F(6,73)$ = 4.53, p < .01. Thus, the final model adequately represented our data. In the final model, the only significant predictors were the two personality class variables (β = .31 and .39, *p*'s < .01).

To evaluate the accuracy of the regression model we examined residual and influential statistics. Five cases (6.25%) had absolute studentized residuals > 1.96 indicating potential influence on the regression model, but none had a Cook's distance > 1. No case had an absolute standardized DFBeta > 2, thus indicating no substantial influence on the regression parameters (26). In order to assess the generalizability of our regression model, we calculated an adjusted R^2 of

0.13 using Stein's formula (26) and assessed several regression assumptions. The Durbin-Watson statistic of d = 1.96 suggested uncorrelated residuals, and a non-significant Kolmogorov-Smirnov test indicated normal distribution of the standardized residuals, $D(80) = 0.07$, $p = .20$. All tolerance values were > .2 implying no potential collinearity problems between the considered predictors, although the average variance inflation factor (VIF) was 1.33.

Table 3. *Results of the multiple regression analysis (with Morbidity Index as the unit of outcome)*

	B (*S.E.*)	β	95% Confidence Interval for *B*
Final Regression Model[a]			
Constant	0.25 (0.13)		[.00, .50]
Vulnerable vs. resilient class	0.23 (0.08)	.31**	[.08, .39]
Highly vulnerable vs. resilient class	0.54 (0.16)	.39**	[.22, .85]

Note. R^2 = .11 for Step 1 (not shown), ΔR^2 = .17 for Step 2 ($p < .01$).

[a] Non-significant predictors: Number of co-morbid diagnoses, Age at onset, Number of past episodes, Previous rapid cycling.

** $p < .01$.

Discussion

Summary of the results

This study is the first prospective investigation to show the impact of personality profiles on the course of BD. We successfully identified subgroups of BD patients based on their NEO-FFI profiles. The resulting 3-class model both represents the sample and sufficiently classifies patient groups. In addition, we observed that a poorer longitudinal outcome based on the MI

was associated with belonging to either the vulnerable or highly vulnerable class. Personality classes accounted for 28% (adjusted $R^2 = .13$) of the variation of the MI.

Discussion of the obtained class solution

Our latent class solution extended upon Wardenaar *et al.'s* (5) study with patients with major depressive disorder by identifying *resilient* and *vulnerable* classes, but also a third, *highly vulnerable* class. Despite methodical similarities, the novelty of the current study findings in a BD sample is noteworthy; particularly given the differences in the personality profiles of unipolar depression versus BD (27, 28). In terms of the obtained class solution, a key point to consider is the definite rejection of the 1-class model, implying that reporting the mean scores for each individual personality scale for the entire sample would be an unacceptable oversimplification of the data. Interestingly, openness to experience was the only personality dimension whereby none of the three detected classes differed. This may be interpreted in line with previous research, which has described openness as a distinct characteristic in patients with BD (29, 30), whereas neuroticism and extraversion for example seem to be nonspecifically related to psychological disorders in general (7).

Previous studies focusing on the link between BD and personality features were mostly limited to the comparison of euthymic patients with healthy control subjects or population norms. While there have been some relatively consistent findings – for example of elevated levels of neuroticism and lower levels of conscientiousness in BD (29, 30) – there is notable disparity in the body of empirical studies. Our study addressed the discrete question as to whether this may be solely due to study characteristics, or rather alternatively, if the homogeneity of BD patients may in fact be a false assumption. Indeed, when BD subgroups have been described in previous studies, some differences emerged: For example, higher neuroticism scores were reported in BD type II vs. type I patients (27, 31).

To validate our three personality classes, we searched for potential associations across a set of clinical variables. Our finding of an association between higher vulnerability and more co-morbid disorders is in line with previous research explaining co-morbidity by neuroticism and conscientiousness (32, 33). Both factors are essential in differentiating our highly vulnerable and resilient class. However, a considerable strength of our naturalistic study is its representativeness: Due to the inclusion of patients with co-morbid diagnoses, the results can be generalized to the majority of BD patients who indeed suffer from at least one additional axis I or II diagnosis (34, 35). In line with the conclusion of Leboyer *et al.* (36) who linked earlier onset age of BD with more severe clinical features and a worse longterm outcome, patients in our vulnerable class reported an earlier onset age compared to the resilient class. The lack of observed difference in age at onset for the highly vulnerable class was not expected, but may be explained by the small size of this subgroup in our study (n = 8).

Discussion of the prospective results: Morbidity Index in BD

The second major finding of our study was that the MI provided crucial clinical information in measuring the prospective illness course and differentiated the three personality classes. The generalizability of our regression model is particularly important if we are to draw conclusions about BD populations beyond the current study's sample; such as for instance the expectation of a poorer treatment outcome for patients with a highly vulnerable personality. The predictive value of the personality variables may be explained by several factors. First, previous research has linked personality – in particular agreeableness – and treatment outcome by means of its effects on the therapeutic alliance (37). In this way, certain combinations of specific traits may serve as an asset or obstacle to the therapeutic intervention. According to Miller (38), high neuroticism indicating emotional instability may underlie an instable, poorer clinical course, with destabilizing effects in stressful situations or phases of life. Low extraversion may lead to

withdrawing from or having reservations in relationships, thus results in the absence of social support which in turn triggers or maintains depression; while high extraversion conversely may be associated with positive coping behavior (39). It is plausible that low conscientiousness may be related to a lack of investment in treatment.

While the utilization of the MI as an indicator of prospective illness course is still a relatively novel approach, it is advantageous over many of the most widely-used single measures (e.g., number of affective episodes, hospitalizations, time to remission or time to relapse). The MI considers both the duration of an affective illness episode, as well as the severity of depressive and/or (hypo-)manic symptoms. Our modified MI additionally integrates subthreshold symptomatology, and thus considers impairments that are relatively unique or specific to BD beyond acute psychopathology (16). The use of the MI might serve as a core asset in predicting clinical courses of BD by personality aspects where past studies using single measures failed to do so (e.g., 40).

Methodical considerations & limitations of the study

Some particular limitations should be considered in interpreting the study's findings. The relatively small sample size and the size of the third class in the model produced should be kept in mind. However, this group was retained as our subsequent analyses showed a unique set of clinical correlates, emphasizing the conceptual gain of considering the highly vulnerable class. Notably, our sample included only euthymic patients: We excluded over 40 participants to minimize the risk of current mood states as possible confounders for personality scores. The five factors of the NEO-FFI investigate personality features on a very broad and abstract level. Without information on the lower facet levels, clinical interpretations drawn could be considered vague and thus less meaningful. Conversely, we found several clinical variables related to the detected NEO-FFI-based latent classes.

The cross-sectional nature of our personality assessment limits the interpretability of the findings in terms of interdependency with the illness course. They may be interpreted in accordance to the *pathoplasticity* model as described by Klein et al. (1), where belonging to a more vulnerable class indicates a risk factor for a more severe and poorer course of bipolar disorder. However, pre-morbid data or personality assessment later in the course of the illness are lacking here, and thus conclusive arguments against the *common cause* or *complication model* cannot be drawn. To minimize *state-dependent influences* of psychopathology on personality assessment we included only euthymic patients in our analyses, given the evidence that personality assessments are biased by current mood state in depressive patients (41, 42). Our classes still significantly differed in their level of depressive symptoms, where higher Hamilton Depression ratings were associated with higher vulnerability. Thus, potential subclinical depressive mood confounds cannot be completely eliminated. Interestingly, Wardenaar *et al.* (5) found similar latent personality profiles in patients suffering from acute major depressive episodes which may indicate a psychopathological influence rather on the profile level than on the profile shape. Our regression model showed that, in contrast to the personality class variables, clinical variables did not predict the illness course. While there was notable variability in the patient observation times in our study, studies following BD patients for up to a period of two years such as in the current study are rare. It is recommended that future researchers employ longitudinal designs in order to assess the potential interdependencies of personality features and BD.

Clinical implications & Conclusion

A key strength of the presented approach is the interpretability of a single typology over and above the consideration of several independent personality dimensions. This approach arguably has the potential to simplify communication between professionals supporting patients in clin-

ical care. Indeed, it also has the scope to improve communication between patients and caregivers in the context of providing psychoeducation. According to our results, it may be possible to anticipate the course of a patient's illness based on individual personality features. Consequently, a brief personality screening may also become a heuristic part of the initial assessment process for the early detection of BD. This would reduce delays in diagnosis and, accordingly, reduce the likelihood of negative consequences associated with lack of detection, e.g., self-harm, co-morbidities, reduced ability to attain age-specific developmental tasks or inadequate treatment decisions (43), and overall illness burden.

Neuroticism is associated with mixed states (44) and can contribute to the experience of more adverse life events (45). Ogrodniczuk *et al.* (46) found extraversion, openness, conscientiousness and low neuroticism to predict a positive treatment outcome in group psychotherapy; a profile clearly akin to our resilient personality class. In contrast, specialized treatment has been found to result in quicker recovery in vulnerable – but not in resilient – patients (5). Collectively, these findings indicate that patients with a resilient personality profile may be predestined for more efficient, low-threshold interventions (e.g., group therapy), while more vulnerable patients tend to profit from more intensive and individually-tailored treatments which are more effective at preventing the development of a more severe disease trajectory.

The extraction of latent personality classes in BD patients again underlines the heterogeneity of the disorder. Groups of patients in the bipolar spectrum sharing specific personality features are characterized by similar clinical courses. Despite its widespread utilization in personality psychology, the Five Factor Model still lacks findings in specific areas of clinical psychology. Particularly in the context of BD, empirical evidence is rare. Using a prospective study design and latent profile analysis, this study makes a valuable contribution by linking the personality research tradition of the five factor model to an applied clinical cohort, offering meaningful clinical implications regarding the prospective prediction of illness courses.

Abbreviations

BD: Bipolar Disorder; HDRS-21: Hamilton Depression Rating Scale – 21 item version; MI: Morbidity Index; NEO-FFI: NEO Five Factor Inventory; YMRS: Young Mania Rating Scale.

Declarations

Ethics approval and consent to participate

All the procedures were conducted in accordance with the 1975 Declaration of Helsinki for ethical principles in medical research. Procedures were also approved by the ethics committees of each of the participating study centers.

Consent for publication

Not applicable.

Availability of data and materials

The data sets generated and/or analysed during this study are not publicly available because participants did not agree to share their clinical data as an open source. They are, however, available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

TS, AF & MB conceptualized and designed the larger multicentre prospective study and were responsible for the management of the data in the larger study. EQ, NO, JR & AD developed the research questions. NO carried out the statistical analyses, data interpretation and drafted the initial manuscript. NO, JR & AD prepared, reviewed and monitored the dataset. SF, CS, AF, BK were responsible for the management of the data. All authors contributed to the editing and revision process, in particular GOM. All authors read and approved the final manuscript.

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Figures

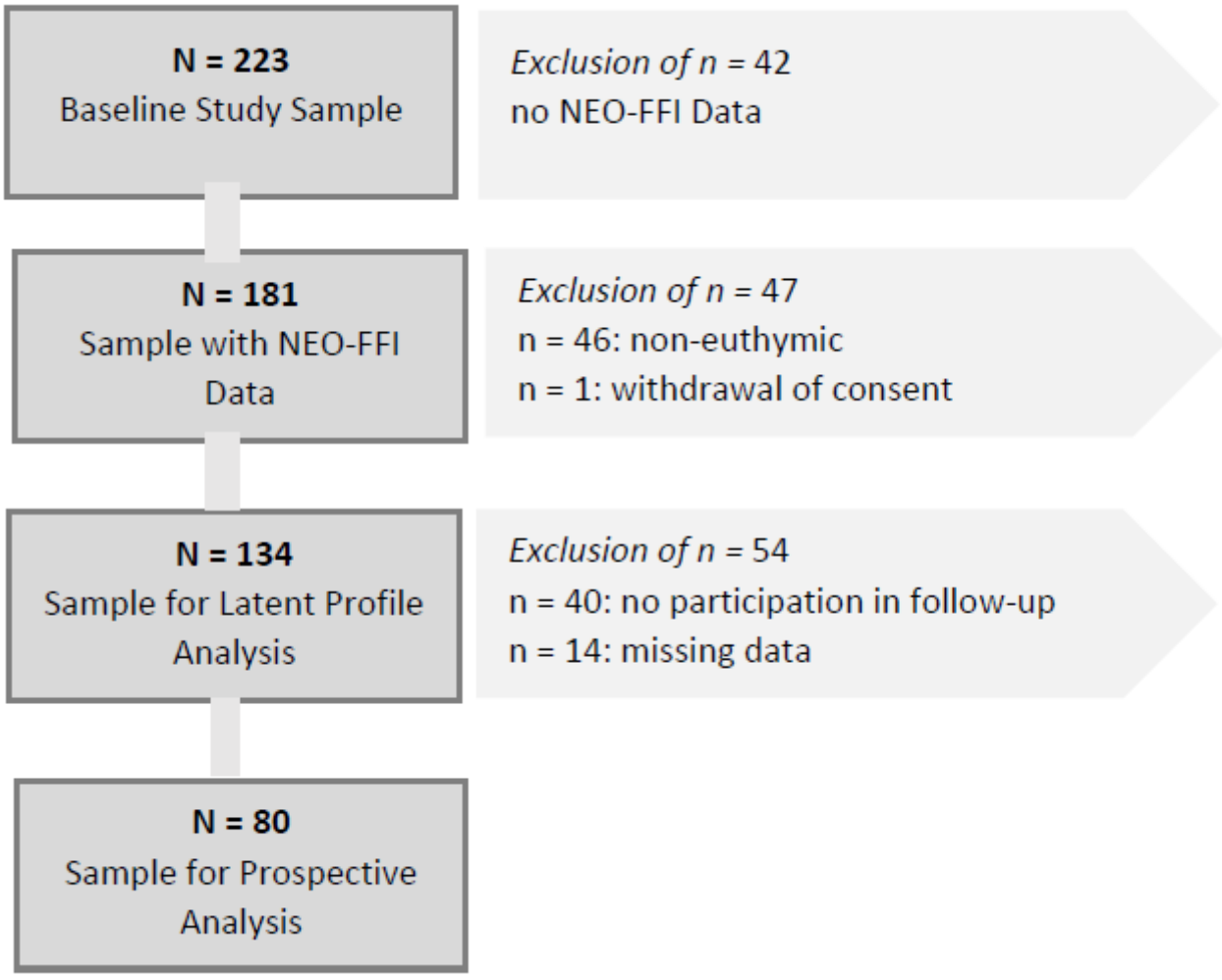

Figure 1

Flowchart displaying exclusion of patients and resulting sample sizes. NEO-FFI, NEO-Five Factor Inventory.

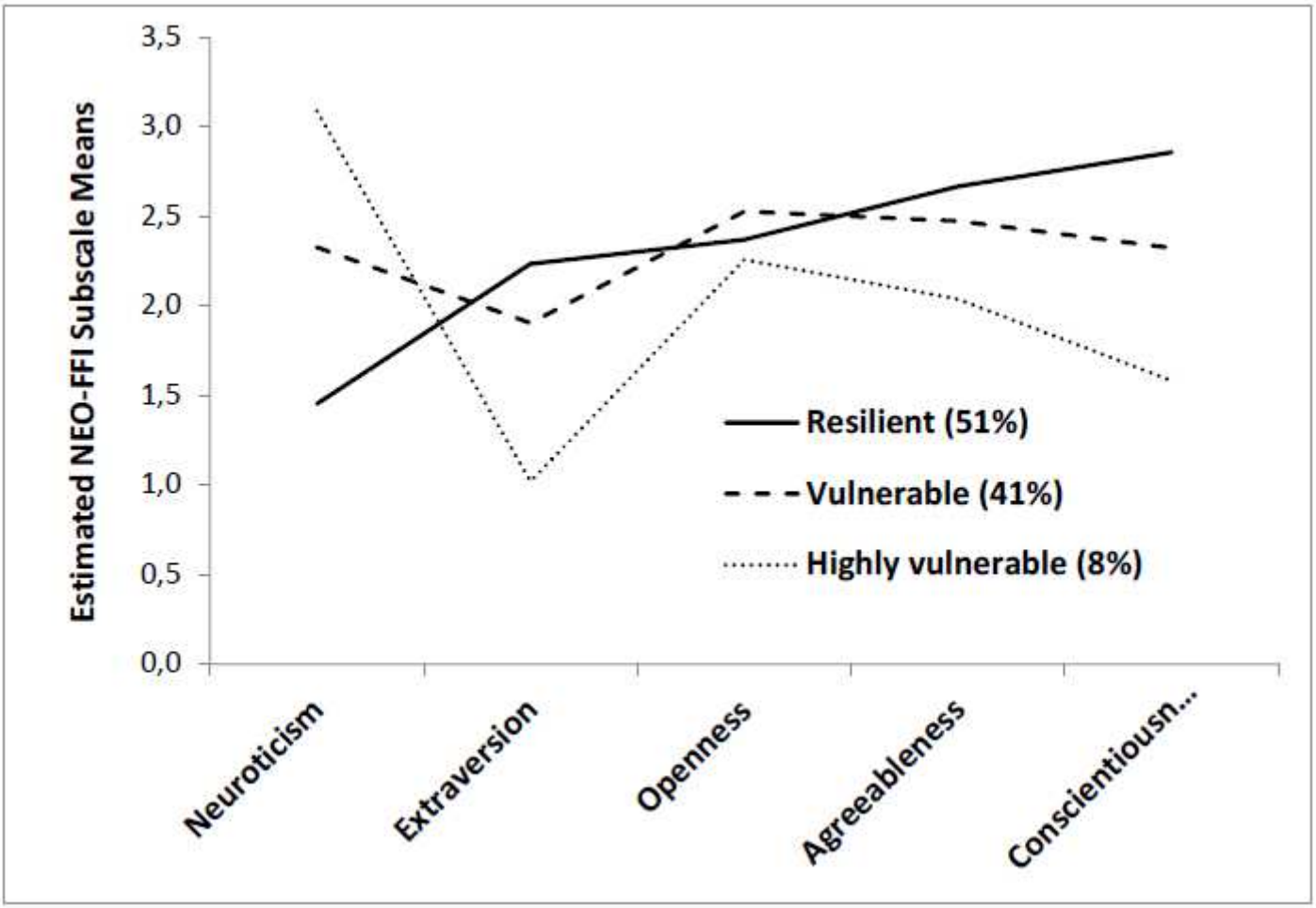

Figure 2

Class-specific personality profiles for the 3-class model. NEO-FFI, NEO-Five Factor Inventory.