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Personality traits differentiate patients with bipolar disorder and healthy controls
- a meta-analytic approach

Persönlichkeitsmerkmale unterscheiden Patienten mit bipolarer Störung und gesunde Kontrollpersonen
- ein meta-analytischer Ansatz

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Glossary

BD	Bipolar Disorder
HC	Healthy Controls
FFM	Five Factor Model
TFM	Three Factor Model
N	Neuroticism
E	Extraversion
P	Psychoticism
O	Openness
C	Conscientiousness
A	Agreeableness
MDD	Major Depressive Disorder
OCD	Obsessive Compulsive Disorder
SCZ	Schizophrenia
BD I	Bipolar Disorder Type I
BD II	Bipolar Disorder Type II
NOS	Not Otherwise Specified
DSM	Diagnostic and Statistical Manual of Mental Disorders
ICD	International classification of diseases
CI	Confidence Interval
BFI	Big Five Inventory
EPI	Eysenck Personality Inventory
EPQ(-R)	Eysenck Personality Questionnaire(-Revised)
MPI	Maudsley Personality Inventory
NEO-FFI	NEO Five-Factor Inventory

NEO-PI-R	Revised NEO Personality Inventory
SSP	Swedish universities Scales of Personality
ZKPQ	Zuckerman-Kuhlman Personality Questionnaire
GWAS	Genome-Wide Association Studies
s.e.	standard error
HitTOP	Hierarchical Taxonomy Of Psychopathology
GWAS	genome-wide association studies

1 Summary

1.1 Summary (english)

Many studies have correlated particular personality traits with the manifestation and progression of bipolar disorder (BD). Still, results to date have been conflicting, because of factors such as age, sex, and limited sample sizes. These differences make it difficult to draw conclusions from the previous results.[1]

We conducted a meta-analysis of individuals with BD and healthy controls (HC) to clarify the role of personality traits in BD and to overcome these limitations. We focused on personality traits defined by the "big three" and "big five": Neuroticism (N), Agreeableness (A), Extraversion (E), Conscientiousness (C), Openness (O) and Psychoticism (P).[1]

We systematically searched two online databases (Pubmed and Web of Science) for articles up to December 31, 2019, to identify relevant articles. We analyzed data from 18 eligible studies, which involved a total of 1694 patients with BD and 2153 HC. In addition, we conducted moderator analysis for age, sex, quality score and publication year to determine their impact on effect sizes.[1]

Our results showed that BD patients scored higher in N; n = 18, g = 1.44 (large positive effect size), with a 95% confidence interval between 1.11 and 1.77. Scores on C and E were associated with negative effect sizes; C: n = 6, g = -0.78 (medium negative effect size), with a 95% confidence interval between -1.13 and -0.43; E: n = 13, g = -0.38 (small negative effect size), with a 95% confidence interval between -0.52 and -0.23.[1]

Our research revealed that the average age of the sample had an impact on the effect size of N, with a reduced distinction in N scored between BD patients and HC among older individuals (-0.0437, z = - 3.96, p <.0001). The results were solid und immune to possible biases and potential confounders including gender, age, quality score and year of publication.[1]

However, subgroup analysis regarding the influence of mood states and BD subtypes could not be conducted due to lack of available data. Furthermore, our analysis was based on cross-sectional data, and therefore, caution should be exercised when interpreting the results, particularly in terms of causality.[1]

Our findings showed that patients with BD displayed different expressions of personality traits than HC. These findings lay the foundation for future investigations focusing on personality and psychopathology in BD. Further exploration of the interplay between personality traits and BD could open up new opportunities for prevention and treatment.[1]

1.2 Zusammenfassung (deutsch)

Die Ausprägung bestimmter Persönlichkeitsmerkmale wurde in mehreren Studien mit dem Auftreten und dem Krankheitsverlauf einer bipolaren Störung (BD) in Verbindung gebracht. Bis heute sind die Ergebnisse jedoch uneinheitlich und potenziell beeinflussende Faktoren wie Alter und Geschlecht, sowie der begrenzte Stichprobenumfang früherer Studien erschweren eine Verallgemeinerung dieser Ergebnisse. Um diese Einschränkungen zu überwinden und die Rolle von Persönlichkeitsmerkmalen im Zusammenhang mit der BD zu spezifizieren, führten wir eine Metaanalyse bei Patienten mit BD und gesunden Kontrollpersonen (HC) durch, bei welcher wir uns auf die Merkmale der „Big Three“ und der „Big Five“ konzentrierten: Neurotizismus (N), Extraversion (E), Offenheit (O), Gewissenhaftigkeit (C), Verträglichkeit (A) und Psychotizismus (P).

Um relevante Studien zu identifizieren, wurden zwei Online-Datenbanken (Pubmed und Web of Science) systematisch nach Veröffentlichungen bis einschließlich 31. Dezember 2019 durchsucht. Aus Studien, die unsere Einschlusskriterien erfüllten (n = 18), extrahierten wir relevante Daten von Patienten mit BD (n = 1694) und von HC (n = 2153) und berechneten die Effektgrößen für jedes Persönlichkeitsmerkmal. Außerdem führten wir eine Moderatorenanalyse zu Geschlecht, Alter, Qualitätsbewertung und Erscheinungsjahren durch.

Unsere Ergebnisse zeigen, dass Patienten mit BD im Vergleich zu HC höhere Werte für N (große positive Effektgröße; n = 18, g = 1,44, 95%-CI: 1,11 bis 1,77) und niedrigere Werte für C (mittlere negative Effektgröße; n = 6, g = -0,78, 95%-CI: -1,13 bis -0,43) und E (kleine negative Effektgröße; n = 13, g = -0,38, 95%-CI: -0,52 bis -0,23) aufweisen. Wir fanden einen moderierenden Effekt des Durchschnittsalters auf die Effektgröße von N: es zeigten sich geringere Unterschiede in den N-Werten zwischen Patienten mit BD und HC in älteren Stichproben (-0,0437, z = - 3,96, p <.0001). Unsere Ergebnisse waren belastbar in Bezug auf potenzielle

Publikationsverzerrungen sowie unter Einbezug potenziell störender Faktoren wie Geschlecht, Alter, Qualitätsbewertung und Veröffentlichungsjahr.

Aufgrund des Mangels an verfügbaren Daten konnte keine Subgruppenanalyse zur Auswirkung von Stimmungszuständen der Patienten und Subtypen der BD durchgeführt werden. Darüber hinaus basieren unsere Analysen auf Querschnittsdaten, so dass die Ergebnisse, insbesondere im Hinblick auf kausale Schlussfolgerungen, mit Vorsicht zu interpretieren sind.

Patienten mit BD zeigten Unterschiede in mehreren Persönlichkeitsmerkmalen im Vergleich zu HC. Unsere Ergebnisse bilden die Grundlage für künftige Forschungsarbeiten mit Schwerpunkt auf Persönlichkeit und Psychopathologie bei Patienten mit BD. Die Identifizierung der Wechselwirkung zwischen der Ausprägung von Persönlichkeitsmerkmalen und BD könnte neue Ansätze für die Prävention und Therapie liefern.

2 Introduction

The etiology of mental disorders is a complex interplay of various factors such as genetic predisposition and environmental risk factors.[2,3] One of these factors might be personality.[4] Since early times of Hippocrates and Galen with their balance of the four humors [see 5] and later with Freuds' theory of personality,[6] there have been various approaches to explain certain relationships between personality- and psychopathology. By now we are able to compare these investigations due to two reasons: (a) the universal classification systems of mental diseases and (b) the consensus in taxonomy of personality traits.

In the following introduction I will give an overview about BD, its definition and diagnostic criteria, its epidemiology and ethology as well as about its course and prognosis. Further, I will give an insight into the taxonomy of personality and finally emphasize the connection between BD and personality traits. Concluding I will outline the prospects and aims of the publication and this work.

2.1 Bipolar Disorder

2.1.1 Epidemiology and Etiology

The occurrence of bipolar spectrum disorder across different nations has a lifetime prevalence that varies between 1-2%.[7,8] By now the question for causes of development of BD cannot conclusively be answered.[9] A multifactorial genesis is probable: To a relatively strong genetic component are added environmental influences, further personality characteristics might play a decisive role.[9] Already Kraepelin assumed that personality might be an important factor in the genesis, onset, and progression of manic-depressive illness.[1,10] In addition, Jung hypothesized that those who display extraverted tendencies might be prone to manic depression [see 11-14]. Various research groups have examined personality traits exhibited in individuals with BD, since these initial observations.[1,15-21]

2.1.2 Definition and Diagnostic Criteria

BD is an affective illness marked by recurrent and episodic fluctuations in mood, disruption in cognitive functioning, and volatility in social behavior.[1,22]

For the diagnosis of BD, the patient must experience at least one episode of depression and one episode of manic symptoms.[22] **Table 1a** shows DSM 5 diagnostic criteria for major depression, **Table 1b** shows DSM 5 criteria for manic episode. The DSM 5 as well as the ICD-10 distinguish two types of BD (BD I and II).[22,23] For BD I patients must meet criteria of at least one episode of fully developed major depression and of at least one fully developed manic episode. Patients with BD II must experience at least one episode of major depression, but their manic symptoms do not fulfill criteria of fully developed manic episode.[22] Their manic symptoms are less pronounced and never psychotic, so called hypomanic.[22]

Major Depressive Episode- DSM 5 Criteria	
A.	**"Five (or more) of the following symptoms** have been present during the same **2-week period** and represent a change from previous functioning; **at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.** 1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, or hopeless) or observation made by others (e.g., appears tearful). 2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation). 3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month) or decrease or increase in appetite nearly every day. 4. Insomnia or hypersomnia nearly every day. 5. Psychomotor agitation or retardation nearly every day (observable by others; not merely subjective feelings of restlessness or being slowed down). 6. Fatigue or loss of energy nearly every day. 7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick). 8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others). 9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide." [22 (S.125)]
B.	"The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning." [22 (S.125)]
C.	"The episode is not attributable to the physiological effects of a substance or another medical condition." [22 (S.125)]

Table 1a. Diagnostic Criteria for Major Depression of DSM 5 [22 (S.125)]

Manic Episode - DSM 5 Criteria	
A.	"A distinct period of **abnormally and persistently elevated, expansive, or irritable mood** and abnormally and persistently **increased goal-directed activity or energy**, **lasting at least 1 week** and **present most of the day**, nearly every day (or any duration if hospitalization is necessary)." [22 (S.124)]
B.	"During the period of mood disturbance and increased energy or activity, **3 (or more) of the following symptoms (4 if the mood is only irritable)** are present to a significant degree and represent a noticeable change from usual behavior: 1. Inflated self-esteem or grandiosity. 2. Decreased need for sleep (e.g., feels rested after only 3 hours of sleep). 3. More talkative than usual or pressure to keep talking. 4. Flight of ideas or subjective experience that thoughts are racing. 5. Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed. 6. Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation (i.e., purposeless non-goal-directed activity). 7. Excessive involvement in activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)." [22 (S.124)]
C.	"The mood disturbance is sufficiently severe to cause marked impairment in social or occupational functioning or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features." [22 (S.124)]
D.	"The episode is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication, other treatment) or to another medical condition." [22 (S.124)]

Table 1b. Diagnostic Criteria for Manic Episode of DSM 5 [22 (S.124)]

2.1.3 Course and Prognosis

BD is associated with a high rate of relapses, more than 90% of patients who experience a single manic episode go through recurrent mood episodes.[22] Whereby the individual course is very variable.[24] Similar to the causes of development, the course and prognosis of BD is influenced by multiple factors such as environmental, genetic and physiological variables.[22] Different authors proposed that the exhibition of distinct personality characteristics is associated with the course of BD.[1,25,26] Further, premorbid personality traits with inadequate coping strategies are associated with chronic courses.[27]

2.2 Taxonomy of Personality

To reach consensus on the taxonomy of personality traits, it was initially necessary to recognize that personality can be ordered hierarchically, from multiple specific traits to a small number of general traits.[28] This was the fundament for the concretization of the general traits in two prominent theories, that by now are most frequently used in this field - the model of the "Big Five" or the "Five Factor Model

(FFM)" and the "Big Three" or "Three Factor Model (TFM)". They collectively establish six distinctive personality traits: Neuroticism (N), Extraversion (E), Psychoticism (P), Openness (O), Conscientiousness (C), and Agreeableness (A). [1,29-34]

N is the vulnerability to emotional instability and self-consciousness, E is defined as predisposition towards sociability, assertiveness and social interaction, P is the tendency to impulsiveness and impersonality, O describes the cognitive disposition to creativity and aesthetics, C is tendency towards dutifulness and competence, and A depicts the tendency towards being sympathetic, trusting, and altruistic. [1,35,36] Part of both theories are the traits N and E, and they are considered equivalent in both of them.[1,5,37]

The six personality traits were regarded as stable across age groups, across age groups, languages and cultures, as well as self- and peer-assessments.[1,28,33,38] In addition, these personality attributes encapsulate aspects of the individual's character that persist over an extended duration of lifetime.[1,39-41]

2.3 Bipolar Disorder and Personality traits

By now, various independent research groups examined the characteristic personality profiles using the FFM/TFM in individuals with various mental illnesses, for example BD. The findings revealed substantial dissimilarities compared to HC. Most outstanding, BD individuals exhibit higher N values than HC.[1,42-48]

In addition, a longitudinal survey which tracked individuals with BD for a two-year period, found that elevated N levels at baseline predict suicidal and violent behavior and depressed moods.[1,46] Nevertheless, N appears as an essential, but nonspecific risk factor as it is related to several mental illnesses.[1,49] Meta-analyses focusing on other psychiatric diseases like generalized anxiety disorder, major depressive disorder (MDD), obsessive-compulsive disorder (OCD), post-traumatic stress disorder, substance use disorder or schizophrenia (SCZ) have examined higher N levels in all patient groups in compression to HC.[1,50,51]

By now, examinations of other personality traits in patients with BD showed inconsistent results. Several studies report lower E in BD compared to HC, while other authors found no significant difference.[43,47,48,52-54] Likewise, in individuals with BD levels of C and A were reported reduced, as well as not significantly different in

comparison with HC.[47,55] O and P were found to be both, lower and higher in BD in comparison to HC.[1,45,53,54,56]

As personality might have an impact on the onset and/or course of BD, it may be of clinical significance to identify the particular expression of personality traits in those individuals.[1,10,19,46,57] This hypothesis is sustained by the results of a prospective investigation showing that large N and small E scores at baseline are predictions for a depressive characterized course of BD.[1,25]

2.4 Prospects and aims to the publication

Determining distinct personality traits in BD could lay the groundwork for future investigations aimed at detecting potential individuals who are susceptible to BD or a specific manifestation of it. This investigation could hold significant value in treatment and prevention of BD.[1]

Further, several issues make generalization of results on personality traits in BD difficult, such as the influence of age and sex distribution, small sample size in prior investigations as well as unclear control groups. Our aim was to address these issues by conducting a meta-analysis that synthesizes the findings from the extensive literature and highlights differences in personality traits between individuals with BD and HC.[1]

Our hypothesis, based on meta-analyses of other disorders, is that (i) BD patients will exhibit different expressions of personality traits compared to HC, including (ii) higher levels in N and (iii) lower levels in E..[1,50,51,58] We also anticipate (iv) no impact of age or gender, as previously found by Akiskal et al. and Su et al.[1,42,48]

3 Publication

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Research paper

Personality traits differentiate patients with bipolar disorder and healthy controls – A meta-analytic approach

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ABSTRACT

Background: Expression of specific personality traits has been associated with the presence and disease course of bipolar disorder (BD) in multiple studies. However, until today findings are inconsistent and potentially confounding factors such as age and gender as well as the limited sample size of previous studies make it difficult to generalize these findings. To overcome these limitations and to specify the role of personality traits in the context of BD, we performed a meta-analysis in patients with BD and healthy controls (HC), focusing on the traits of the big three and the big five: Neuroticism (N), Extraversion (E), Openness (O), Conscientiousness (C), Agreeableness (A) and Psychoticism (P).

Methods: Two online databases (Pubmed and Web of Science) were searched systematically to identify relevant articles, including publications up to December 31, 2019. From studies that met our inclusion criteria ($n = 18$), we extracted relevant data of patients with BD ($n = 1694$) and HC ($n = 2153$) and calculated effect sizes for each personality trait. Further, we performed moderator analysis on gender, age, quality score and years of publication.

Results: Our results indicate that patients with BD exhibit higher scores on N (*large positive effect size;* $n = 18$, $g = 1.44$, 95%-CI : 1.11 to 1.77) and lower scores on C (*medium negative effect size;* $n = 6$, $g = -0.78$, 95%-CI: -1.13 to -0.43) and E (*small negative effect size;* $n = 13$, $g = -0.38$, 95%-CI: -0.52 to -0.23) compared to HC. We found a moderating effect of mean age on the effect size of N with smaller differences in N levels between patients with BD and HC in older samples (-0.0437, $z = -3.96$, $p < 0.0001$). Our results were robust with respect to potential publication biases and the inclusion of potentially confounding factors such as gender, age, quality score and years of publication.

Limitations: Due to the lack of available data no subgroup analysis on the effect of mood states of patients and subtypes of BD could be performed. Moreover, our analyses are based on cross-sectional data so that findings should be interpreted with care, especially concerning causal conclusions.

Conclusions: Patients with BD showed differences in several personality traits compared to HC. Our results provide the basis for future research with focus on personality and psychopathology in patients with BD. Identifying the interaction between expressions of personality traits and BD might provide novel approaches in prevention and therapy.

1. Introduction

Bipolar disorder (BD) is a mental disorder characterized by episodes with extreme shifts in mood, inconsistency in social behavior and disturbance in cognitive functioning (American Psychiatric Association, 2013a). The lifetime prevalence of bipolar spectrum across different countries ranges from 1 to 2% (Merikangas et al., 2011; Pini et al., 2005). It has been suggested that the expression of specific personality traits is associated with BD and its disease course (Barnett et al., 2011; Murray et al., 2007). Already Kraepelin hypothesized a possible role of personality for the etiology, onset and course of manic-depressive illnesses (Kraepelin, 1921) and Jung suggested that extraverted

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individuals might be vulnerable for manic depression (see (Gilliland and Morgan, 1931; Guilford and Guilford, 1934; McDougall, 1929; Neymann and Kohlstedt, 1929). Since these early observations, several research groups investigated personality characteristics in patients with BD (Bagby et al., 1997; Clayton et al., 1994; Engström et al., 2004; Hirschfeld and Klerman, 1979; Lozano and Johnson, 2001; Platman and Plutchik, 1970; Rowe and Daggett, 1954). By now, numerous independent studies have examined the characteristic personality profiles of patients with BD and found significant differences compared to healthy controls (HC) (Akiskal et al., 2006; Jylhä et al., 2010; Liebowitz et al., 1979; Nowakowska et al., 2005; Sparding et al., 2017; Stringer et al., 2014; Su et al., 2018). While a large number of different theories for the taxonomy of personality traits exist, the most commonly used in the field are the big five model/five factor model (FFM) (Goldberg, 1992, 1990; McCrae and Costa, 1987; Tupes and Christal, 1992) and the big three model/three factor model (TFM) (Eysenck, 1967, 1950). Together they define six personality traits: Neuroticism (N), Extraversion (E), Psychoticism (P), Openness (O), Conscientiousness (C) and Agreeableness (A). The dimensions N and E are part of both theories and are considered as equivalent in both of them (Clark and Watson, 1999; Markon et al., 2005).

All six personality traits were found consistent in different languages and cultures (McCrae and Costa, 1997), in self- or peer-ratings (McCrae and Costa, 1987) and across different age ranges (Digman, 1997). Further, these personality traits capture characteristics of the personality which are often found stable over a long period of lifetime (Cobb--Clark and Schurer, 2012; Conley, 1985; Rantanen et al., 2007). Since then, various research groups investigated the FFM/TFM in patients with different mental disorders, such as BD. Most prominently, patients with BD showed higher N levels than HC (Akiskal et al., 2006; Jylhä et al., 2010; Liebowitz et al., 1979; Nowakowska et al., 2005; Sparding et al., 2017; Stringer et al., 2014; Su et al., 2018). Further, in a longitudinal study that followed patients with BD for two years, elevated N levels at baseline predicted depressive moods as well as suicidal and violent behavior (Sparding et al., 2017). However, N seems to be a crucial, but nonspecific risk factor associated with mental disorders in general (Goldberg, 1996). Meta-analyses which focused on other mental disorders such as major depressive disorder (MDD), generalized anxiety disorder, post-traumatic stress disorder, obsessive-compulsive disorder (OCD), substance use disorder (Kotov et al., 2010) or schizophrenia (SCZ) (Ohi et al., 2016), have shown higher scores on N in all of these patient groups compared to HC. The investigation of other personality traits in BD has so far delivered mixed results. In several studies, E was found lower in BD compared to HC (Jylhä et al., 2010; Smillie et al., 2009; Souza et al., 2014; Stringer et al., 2014), but some authors report no significant difference (Furukawa et al., 1998; Su et al., 2018). Similarly, C and A were found to be decreased or not significantly different in BD compared to HC (Canuto et al., 2010; Stringer et al., 2014). O and P were reported both, higher (Lewis et al., 2009; Souza et al., 2014) and lower in BD (Nowakowska et al., 2005; Smillie et al., 2009) as compared to HC.

Identifying a specific expression of personality traits in patients with BD could be of clinical importance because personality might influence onset and/or course of the disorder (Kraepelin, 1921; Lozano and Johnson, 2001; Sparding et al., 2017; Vinberg Christensen and Vedel Kessing, 2006). This hypothesis is supported by findings from a prospective study indicating that high N and low E levels at baseline are predictors for a depression-prone course of BD (Barnett et al., 2011). Thus, identifying specific personality traits of BD might provide the basis for future research with a focus on identifying potential individuals at risk for BD or at risk of a specific course of BD and thus might be a crucial help in prevention and treatment.

However, a number of issues makes it difficult to generalize findings on personality traits in BD such as confounding factors like age and gender distribution, the limited sample size of previous studies and unclear defined control groups. To address these issues and to synthesize findings across the large body of evidence, we aimed to combine the literature in form of a meta-analysis examining differences in personality traits between patients with BD and HC. Based on meta-analyses focusing on several other disorders (Kotov et al., 2010; Malouff et al., 2005; Ohi et al., 2016), we hypothesized that BD patients (i) show different expressions of personality traits than HC, (ii) have higher scores in N and (iii) show lower scores in E than HC. Further, in accordance with Akiskal et al. and Su et al. we expected (iv) no moderating influence of age and gender effects (Akiskal et al., 2006; Su et al., 2018).

2. Methods

2.1. Literature search

Following recommended guidelines as defined in the PRISMA statement (Moher et al., 2009), we conducted a systematic literature search. We searched for literature published before December 31, 2019 in two online data-bases, PubMed and Web of Science. To identify studies investigating personality traits in BD compared to HC, we used the following search term: ("Neuroticism" OR "Eysenck" OR "Zuckerman" OR "Big Five" OR "NEO*" OR "Personality Questionnaire" AND "bipolar disorder" OR "bipolar" OR "affective disorder"). The reference lists of key papers, relevant published reviews and meta-analyses were scanned for additional eligible papers.

2.2. Inclusion/Exclusion criteria

To be eligible for the present meta-analysis, studies had to: (1) be published in English; (2) be published in a peer-reviewed journal; (3) report original data; (4) investigate a group ($n >= 3$) of patients with BD (bipolar disorder type I (BD I), bipolar disorder type II (BD II) or not otherwise specified (NOS)), diagnosed by a standardized diagnostic instrument (e.g. Diagnostic and Statistical Manual of Mental Disorders (DSM) or International classification of diseases (ICD)); (5) compare these with a group of HC with no reported mental disorder; (6) report the score of a relevant questionnaire that measures personality of the FFM or TFM (Costa and McCrae, 1992a; Eysenck, 1950). Studies were excluded in case patients additionally met criteria for other affective disorders (e.g. MDD) or SCZ. In case studies met inclusion criteria but did not report all relevant data (e.g. standard deviations) or reported mixed group effects, we contacted the corresponding authors via email. After two weeks without response, a reminder email was sent to these authors before deciding to exclude the respective study. Studies that used normative data or general population samples as a control group were excluded, as we strictly focused on HC without any psychiatric diagnoses. In case of overlaps due to patient samples reported in several independent publications, we included the study with the largest sample size.

We used the Newcastle-Ottawa Scale (Wells et al., 2014) to check studies for quality criteria (Supplementary Table 1). All inclusion, exclusion and quality criteria were rated by two independent authors (NH and NP). Discrepancies were discussed with a third author until consensus was reached (LTB).

2.3. Extraction

We extracted mean scores and standard deviations for the six dimensions of the FFM and TFM (O, C, E, A, N and P). If necessary, we derived the effect size from other reported statistics (e.g. t-values, F-values) as specified in the Cochrane Handbook (Higgins et al., 2019). We collected all available data on age, gender and mood state (euthymic, manic, depressed) at the time of testing, type of BD (BDI, BDII or NOS), mean score of Young Mania Rating Scale (Young et al., 1978), mean score of Hamilton Depression Scale (Hamilton, 1960) and years of education. One author (NH) extracted data from eligible articles and a

second author (NP) checked 30% of all data entries randomly.

2.4. Statistical analysis

We conducted a random-effects meta-analysis for each of the six personality traits (O, C, E, A, N and P) to compare the expression of the trait between the two groups in terms of the standardized mean difference (Hedges' g) and calculated 95% confidence intervals (CI). To categorize the effect sizes, we used common cut offs from the literature: small ($g = 0.2$), medium ($g = 0.5$) and large ($g = 0.8$) (Cohen, 2013). We examined and quantified statistical heterogeneity using the Q-test and the I^2-statistic. Further, we calculated funnel plots and forest plots to identify possible heterogeneity between the studies and used Egger's test (Egger et al., 1997) to test for funnel plot asymmetry. We performed outlier-analysis for each trait to identify single study results driving the effect sizes (Viechtbauer and Cheung, 2010). In case of outliers, we performed a second analysis of the trait after removing these outlying studies. To examine moderating effects of mean age, gender distribution, quality score and year of publication we used meta-regression (using a mixed-effects model). Finally, we conducted moderator analyses for traits that included at least 10 studies reporting the variable of interest. We performed all steps of the meta-analysis using the 'metafor' package (Viechtbauer, 2010) of *R* Version 3.6.1 (R Core Team, 2019). This meta-analysis was registered publicly on April 27, 2020 at OSF-Registries (https://osf.io/876ky).

3. Results

3.1. Study selection

We identified 954 articles in Pubmed and Web of Science. After removing duplicates, we included 739 studies for screening. Using cross-referencing, we identified 2 additional studies. Following our pre-specified exclusion criteria, we included 18 studies with a total of 1694 patients with BD and 2153 HC (Akiskal et al., 2006; Bauer et al., 2016; Canuto et al., 2010; Furukawa et al., 1998; Güleç et al., 2008; Jylhä et al., 2010; Lewis et al., 2009; Liebowitz et al., 1979; Lövdahl et al., 2014; Nowakowska et al., 2005; Rothen et al., 2009; Roy, 1990; Smillie et al., 2009; Souza et al., 2014; Sparding et al., 2017; Stringer et al., 2014; Su et al., 2018; Xu et al., 2015). Fig. 1 shows the flow diagram with the different stages of our systematic literature search.

In total, we contacted the authors of 26 articles for additional information. Fourteen of them did not report results for patients with BD separately, but for different patient groups combined (e.g. BD and MDD). Twelve did not report all relevant data (e.g. no standard deviations). Overall, 9 authors replied. Three of them did not measure data meeting our inclusion criteria and 4 no longer had access to the relevant data. Two authors shared the specific data with us, so that we could include their studies. Included studies used a total of 8 questionnaires: Big Five Inventory (BFI) (John and Srivastava, 1999), Eysenck Personality Inventory (EPI) (Eysenck, 1964), Eysenck Personality

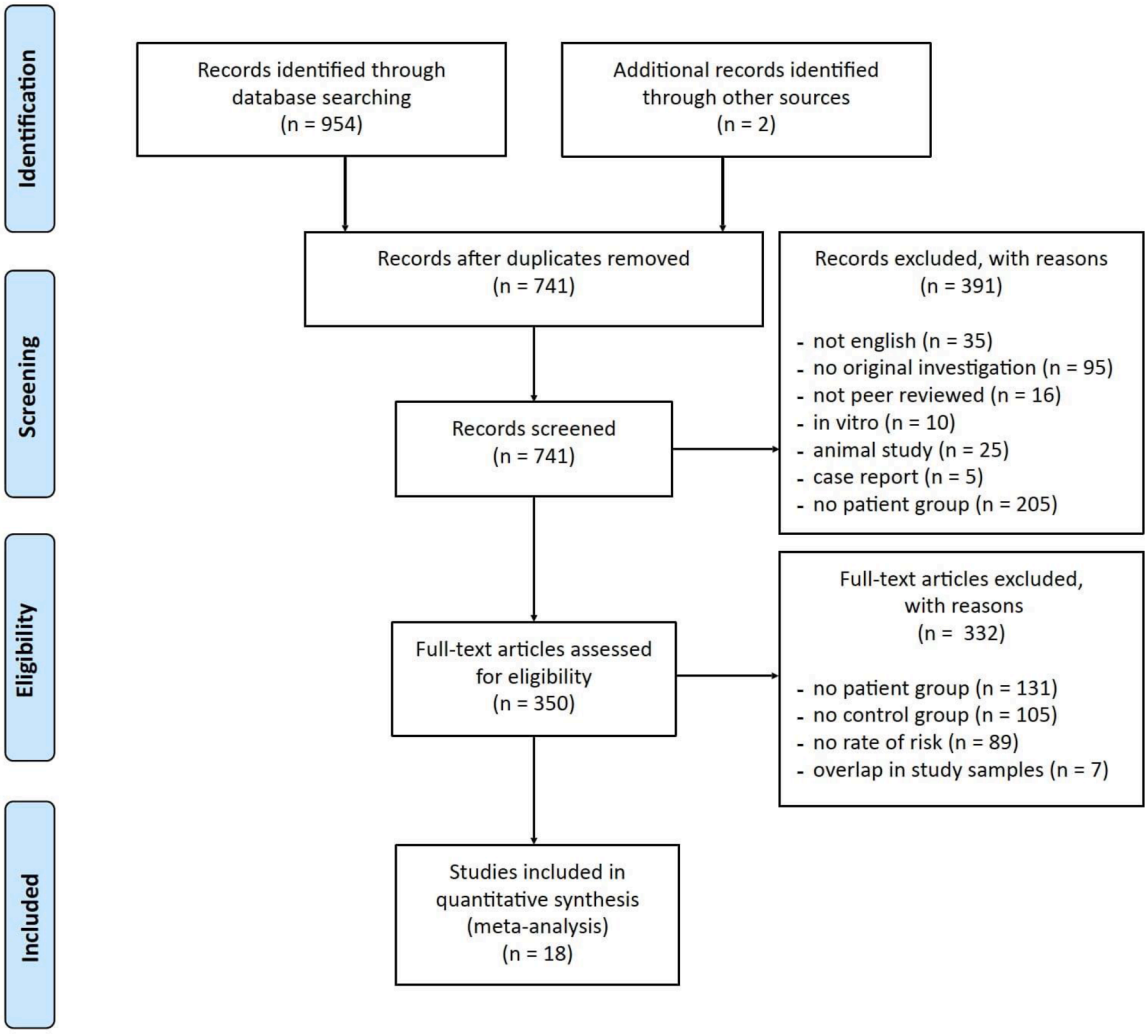

Fig. 1. Flow diagram according to PRISMA guidelines (Moher et al., 2009).

Questionnaire(-Revised) (EPQ(-R)) (Eysenck and Eysenck, 1984, 1975), Maudsley Personality Inventory (MPI) (Eysenck, 1962), Neo Five-Factor Inventory (NEO-FFI) (Costa and McCrae, 1992a), Revised NEO Personality Inventory (NEO-PI-R) (Costa and McCrae, 1992b), Swedish universities Scales of Personality (Gustavsson et al., 2000) (SSP) and Zuckerman-Kuhlman Personality Questionnaire (ZKPQ) (Zuckerman et al., 1993). All questionnaires measure at least one of the FFM or TFM personality traits. All 6 traits measured by these questionnaires can be seen as comparable between those questionnaires (Aluja et al., 2004; Ferrando, 2001; Gosling et al., 2003; McCrae and Costa, 1985). Characteristics of the samples are shown in Table 1. Data on N was available for all 18 studies. Further, 13 studies reported data on levels of E, 6 studies reported data on O, C and A. P was reported in 4 studies.

3.2. Effect sizes and heterogeneity

Meta-analyses indicated higher levels of N, O and P and lower levels of A, E and C in patients with BD compared to HC (Fig. 2).

These results were significant for N, C and E (Fig. 2 and Table 2). Specifically, we found a large positive effect size for N ($n = 18$, $g = 1.44$, 95%-CI: 1.11 to 1.77, $z = 8.59$, $p < 0.0001$, Q(17) = 120.21, $p < 0.0001$, $I^2 = 92.61\%$, Egger's test: $z = 1.56$, $p = .1184$, Table 2 and Fig. 3a). Further, we found a medium negative effect size for C ($n = 6$, $g = -0.78$, 95%-CI: −1.13 to −0.43, $z = -4.37$, $p < .0001$; Q(5) = 14.96, $p = .0105$, $I^2 = 70.65\%$, Egger's test: $z = -1.61$, $p = .1065$, Table 2 and Fig. 3b) and a small negative effect size for E ($n = 13$, $g = -0.38$, 95%-CI: −0.52 to −0.23, $z = -5.13$, $p < .0001$; Q(12) = 22.38, $p = .0335$, $I^2 = 45.20\%$, Egger's test: $z = -0.12$, $p = .9042$, Table 2 and Fig. 3c).

Meta-analyses did not indicate significant differences in the expression of O ($n = 6$, $g = 0.03$, 95%-CI: −0.28 to 0.33, $z = 0.19$, $p = .8503$, Q(5) = 12.54, $p = .0281$, $I^2 = 63.72\%$ Egger's test: $z = -0.26$, $p = .7949$, Table 2 and Fig. 3d), A ($n = 6$, $g = -0.17$, 95%-CI: −0.33 to −0.01, $z = -2.03$, $p = .0421$; Q(5) = 6.50, $p = .2602$, $I^2 = 0.00\%$, Egger's test: $z = -1.23$, $p = .2203$, Table 2 and Fig. 3e) and P ($n = 4$, $g = 0.17$, 95%-CI: −0.29 to 0.64, $z = 0.75$, $p = .4542$; Q(3) = 7.51, $p = .0574$, $I^2 = 60.62\%$, Egger's test: $z = 0.67$, $p = .5007$, Table 2 and Fig. 3f) between patients with BD and HC. Tests for heterogeneity indicated heterogeneity in all traits except for A and P. N showed considerable, C and O substantial and E moderate heterogeneity (Table 2). Regression test for funnel plot asymmetry did not indicate any evidence of publication bias (all $ps > 0.1065$) (Table 2 and Supplementary Fig. 1a–f).

3.3. Outlier analysis

Outlier analysis identified outliers in O, E, A and P. For these traits we repeated the analyses after removing studies that were identified as outliers. After removal of outliers, results for E were found significant, while results for O, A and P were not found significant (small negative effect size for E: $n = 11$, $g = -0.37$, 95%-CI: −0.50 to −0.23, $z = -5.36$, $p < 0.0001$, Q(10) = 9.24, $p = .5098$, $I^2 = 0.00\%$; O: $n = 4$, $g = 0.06$, 95%-CI: −0.13 to 0.25, $z = 0.63$, $p = .5227$, Q(3) = 0.36, $p = .9474$, $I^2 = 0.00\%$; A: $n = 5$, $g = -0.20$, 95%-CI: −0.50 to 0.09, $z = -1.35$, $p = .1765$, Q(4) = 6.50, $p = .1646$, $I^2 = 36.62\%$; P: $n = 2$, $g = 0.16$, 95%-CI: −0.26 to 0.59, $z = 0.75$, $p = .4522$, Q(1) = 0.45, $p = .5007$, $I^2 = 0.00\%$; Table 3, Supplementary Figs. 2a-d and 3a-d). Further, we did not find significant heterogeneity in any of the 4 traits ($p > .1646$) (Table 3).

3.4. Subgroup- and moderator-analysis

We calculated moderator analysis for mean age, quality score and year of publication on the effect size of N and E and for gender distribution on the effect size of N. Moderator analysis showed that mean age was a significant moderator on the effect size of N (−0.04, $z = -3.96$, $p < 0.0001$), i.e., higher mean age in the sample was associated with smaller differences in N between patients with BD and HC. Mean age on the effect size of E and gender distribution on the effect size of N showed no significant moderator effects. Further, neither quality score nor year of publication did show significant moderator effects on the effect size of

Table 1
Demographic data of the studies including in the present meta-analyses. *Notes:* -, not applicable. BD-I/BD-II (%), Bipolar disorder I/II in%. TW, Taiwan. SE, Sweden. USA, United States of America. CN, China. NO, Norway. BR, Brazil. CH, Switzerland. FI, Finland. UK, United Kingdom. TR, Turkey. JP, Japan. EPQ(-R), Eysenck Personality Questionnaire(-Revised) (Eysenck and Eysenck, 1984, 1975). SSP, Swedish universities Scales of Personality (Gustavsson et al., 2000). BFI, Big Five Inventory (John and Srivastava, 1999). ZKPQ, Zuckerman-Kuhlman Personality Questionnaire (Zuckerman et al., 1993). NEO-PI-R, Revised NEO Personality Inventory (Costa and McCrae, 1992b). EPI, Eysenck Personality Inventory (Eysenck, 1964). NEO-FFI, Neo Five-Factor Inventory (Costa and McCrae, 1992a). MPI, Maudsley Personality Inventory (Eysenck, 1962). DSM-III to IV, Diagnostic and Statistical Manual of Mental Disorders - third to fifth edition (American Psychiatric Association, 2013b). ICD-10, International classification of diseases - tenth revision (Organization et al., 2009). RDC, Research diagnostic criteria (Spitzer et al., 1978). Feighner Criteria, Diagnostic criteria for use in psychiatric research (Feighner et al., 1972).

Bipolar (n = 1694)	Healthy Control (n = 2153)										
Authors	Year	Country	Questionnaire	Diagnostic Criteria	BD-I/BD-II (%)	n	Age, mean (SD)	Male, N (%)	n	Age, mean (SD)	Male, N (%)
Su et al.	2018	TW	EPQ-R	DSM-IV	-/-	365	40.9 (13.3)	163 (44.7)	315	42.3 (11.6)	97 (30.8)
Sparding et al.	2017	SE	SSP	DSM-IV	56.4/43.6	195	38.5 (13)	68 (34.9)	86	38 (14)	38 (44.2)
Bauer et al.	2016	USA	BFI	DSM-IV	100/0	14	-	-	22	-	-
Xu et al.	2015	CN	ZKPQ	DSM-V	51.1/48.9	45	22.7 (6.1)	13 (28.9)	64	23.6 (5.9)	26 (40.6)
Lövdahl et al.	2014	NO	EPQ	DSM-IV	0/100	21	35.9 (9.2)	6 (28.6)	21	33.7 (7.5)	6 (28.6)
Souza et al.	2014	BR	NEO-PI-R	DSM-IV	57.1/42.9	35	42.9 (13.8)	7 (20)	40	33.6 (11)	20 (50)
Stringer et al.	2014	USA	NEO-PI-R	DSM-IV	-/-	266	38.2 (13)	98 (36.8)	108	32.5 (14)	51 (47.2)
Canuto et al.	2010	CH	NEO-PI-R	DSM-IV	50/50	22	68.5 (5.5)	12 (54.5)	62	71.1 (7.2)	13 (21)
Jylhä et al.	2010	FI	EPI	DSM-IV	51.6/48.4	188	37.7 (12.1)	89 (47.3)	347	42.9 (11.2)	78 (51.3)
Lewis et al.	2009	UK	EPQ	DSM-IV	90.6/9.4	106	50 (10)	-	30	48.6 (10.5)	-
Rothen et al.	2009	CH	EPQ	DSM-IV	-/-	34	40.9 (6.3)	-	27	-	-
Smillie et al.	2009	UK	EPQ-R	DSM-IV/ICD-10	-/-	50	29.8 (4.1)	25 (50)	50	25.2 (4.8)	25 (50)
Gülec et al.	2008	TR	EPQ-R	DSM-IV	-/-	39	-	-	178	-	-
Akiskal et al.	2006	USA	MPI	RDC	60.5/39.5	162	36.6 (12.4)	65 (40.1)	617	43.2 (17)	284 (46)
Nowakowska et al.	2005	USA	NEO-PI-R	DSM-IV	-/-	49	37.5 (10.8)	18 (36.7)	47	33.8 (14.2)	18 (38.3)
Furukawa et al.	1998	JP	NEO-FFI	ICD-10	-/-	8	-	-	84	41.2 (16.5)	43 (51.2)
Roy et al.	1990	USA	EPQ	DSM III	-/-	6	-	0 (0)	42	39.3 (14.2)	18 (42.9)
Liebowitz et al.	1979	USA	MPI	Feighner Criteria	49.4/30.3	89	47.3 (13.1)	41 (46.1)	13	44.4 (18.1)	3 (23.1)

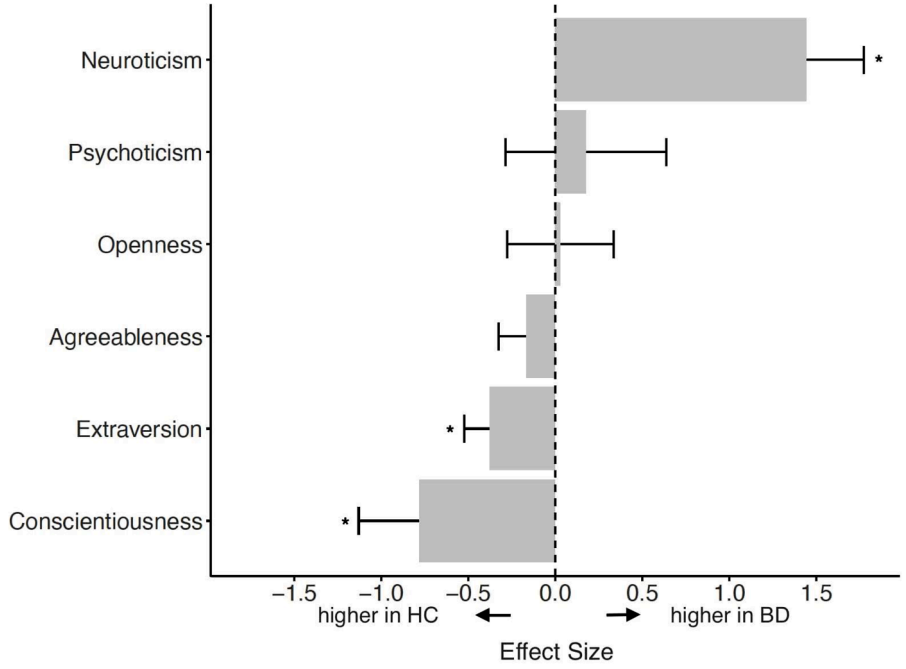

Fig. 2. X-axis: Effect size (Hedges' g), Y-axis: Personality Trait, Error Bars: 95%-Confidence Interval.* indicate significant results ($p < .0001$).

Table 2
Summary of Meta-analysis results, Test for Heterogeneity and Eggers's test. *Notes: n*, number of studies. *g*, Hedges' g. CI, Confidence-Interval. *z*, z-value. *p*, p-value. Q, Cochran's Q. Higgins I^2, heterogeneity in%.

	Meta-analysis results	Test for Heterogeneity		Egger's test						
Trait		*n*	*g*	95%-CI	*z*	*p*	Q	*p*	I^2	*z*
Neuroticism	18	1.44	[1.11, 1.77]	8.59	<0.0001	Q(17) = 120.21	<0.0001	92.61%	1.56	.1184
Psychoticism	4	0.17	[−0.29, 0.64]	0.75	0.4542	Q(3) = 7.51	0.0574	60.62%	0.67	.5007
Openness	6	0.03	[−0.28, 0.33]	0.19	0.8503	Q(5) = 12.54	0.0281	63.72%	- 0.26	.7949
Agreeableness	6	- 0.17	[−0.33, −0.01]	- 2.03	0.0421	Q(5) = 6.50	0.2602	0.00%	- 1.23	.2203
Extraversion	13	- 0.38	[−0.52, −0.23]	- 5.13	<0.0001	Q(12) = 22.38	0.0335	45.20%	- 0.12	.9042
Conscientiousness	6	- 0.78	[−1.13, −0.43]	−4.37	<0.0001	Q(5) = 14.96	.0105	70.65%	- 1.61	.1065

N or E. Due to the limited number of studies that reported data on types of BD, mood states and years of education we did not conduct subgroup analyses on any of these subgroups.

4. Discussion

4.1. Findings and context

In this meta-analysis, we systematically compared personality traits as defined by the FFM and the TFM between patients with BD and HC. Including 18 studies with a total of 1694 patients with BD and 2153 HC, we found differences in personality traits between patients with BD and HC. Three of the investigated personality traits differed significantly among the two groups (N, C and E). As hypothesized, patients with BD scored higher in N (large positive effect size) and lower in E (small negative effect size) than HC. C levels were found lower in BD than in HC (medium negative effect size). Additionally, we found a moderating effect of mean age on the effect size of N: differences in N levels between patients with BD and HC were smaller the younger the sample group was. Importantly, these results were robust with respect to potential publication biases and the inclusion of confounding factors (including year of publication and study quality).

We found a large positive effect size for N, indicating increased levels of N in BD compared to HC. This meta-analytic finding corroborates estimates of individual studies reported in the published literature (Akiskal et al., 2006; Jylhä et al., 2010; Liebowitz et al., 1979; Nowakowska et al., 2005; Sparding et al., 2017; Stringer et al., 2014; Su et al., 2018). Overall, it has been reported that high N has the strongest links to negative emotional experience. It correlates with many specific negative emotional states such as fear/anger, guilt/dissatisfaction, fear/anxiety (Watson et al., 1999; Watson and Clark, 1992; Watson and Naragon-Gainey, 2014; Watson and Naragon, 2009). Unexpectedly several authors found high N in BD not only closely related to depression, but to all dimensions of bipolar symptoms: to depressive symptoms (Heerlein et al., 1998; Lozano and Johnson, 2001; Quilty et al., 2009) as well as to manic symptoms (Quilty et al., 2009).

An explanation for these correlations between N and BD might be found in hypotheses by Murray et al. (2007). They emphasized the link between N and BD based on their similar characteristics: Instability of mood, behavior and cognitive operations are crucial elements of both N (Moskowitz and Zuroff, 2004; Murray et al., 2002; Robinson and Tamir, 2005) and BD (Gottschalk et al., 1995; Judd et al., 2003).

Further, we found a small negative effect size for E. Some of the individual studies included in our metaanalysis found lower E levels compared to those of HC (Jylhä et al., 2010; Smillie et al., 2009; Souza et al., 2014; Stringer et al., 2014), while other studies reported no significant difference (Furukawa et al., 1998; Su et al., 2018). There is evidence that the role of E may be specific to certain mood states of BD: while low E was found in patients during depressive mood states, high E was found in those with a manic mood state (Barnett et al., 2011; Quilty et al., 2009). Due to the lack of available data, differences between certain mood states could not be examined, thus we cannot consider if

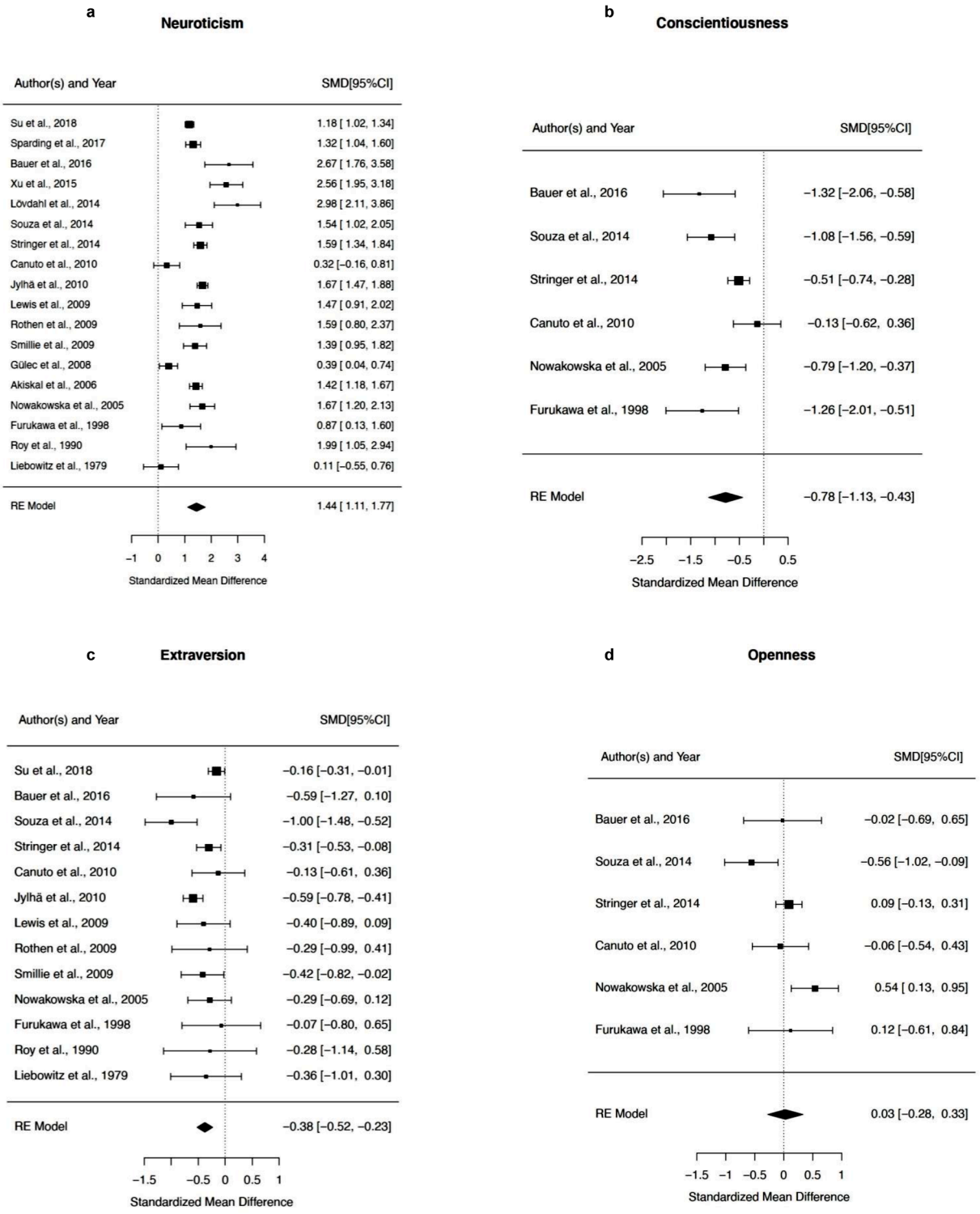

Fig. 3. a–f. Forest plots. *Notes:* SMD, Standard mean difference. CI, Confidence Interval.

our results were driven by certain mood states. Further, BD possibly relates differently between facets of E: Watson et al. found positive correlation between mania symptoms and extraversion facet scales (assessing excitement seeking and venturesomeness) (Watson et al., 2019). As available data regarding different facets of personality traits was limited, a more detailed synthesis was not possible in the present meta-analysis.

Additionally, we found medium negative effect size for C in this meta-analysis. Some of the included studies found lower C levels in patients with BD compared to HC (Souza et al., 2014; Stringer et al., 2014), while there was no significant difference between BD and HC in another study (Canuto et al., 2010). Besides relevant effects in mental health, published literature indicates that low C levels are also of crucial importance in physical health. Thus, low C levels were found to correlate with behaviours that lead to poor physical health and thus were found as the strongest predictor of mortality (Bogg and Roberts, 2004; Roberts

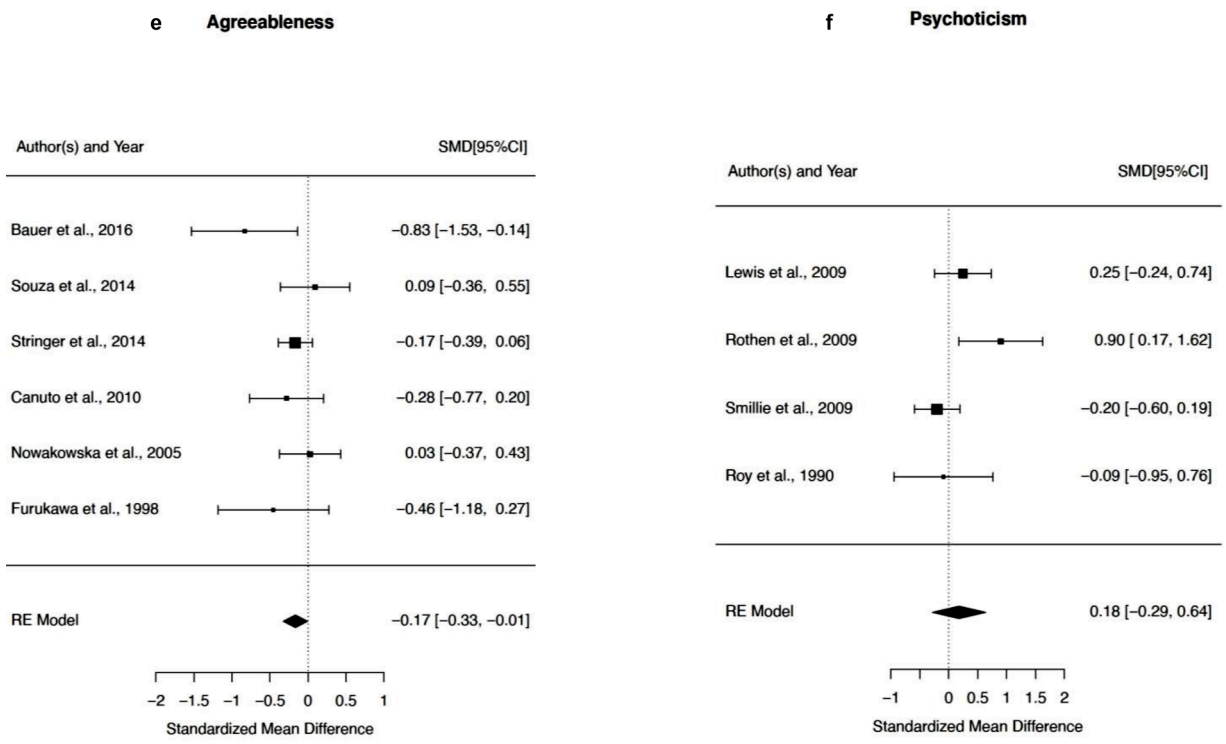

Fig. 3. (*continued*).

Table 3
Meta-analysis Results and Test for Heterogeneity after removal of outliers. *Notes: n*, number of studies. *g*, Hedges' g. CI, Confidence-Interval. *z*, z-value. *p*, p-value. Q, Cochran's Q. Higgins I^2, heterogeneity in%.

Meta-analysis results			Test for Heterogeneity					
Trait	*n*	*g*	95%-CI	*z*	*p*	Q	*p*	I^2
Extraversion	11	- 0.37	[−0.50, −0.23]	- 5.36	<0.0001	Q(10) = 9.24	0.5098	0.00%
Openness	4	0.06	[−0.13, 0.25]	0.63	0.5227	Q(3) = 0.36	0.9474	0.00%
Agreeableness	5	- 0.20	[−0.50, 0.09]	1.35	0.1765	Q(4) = 6.50	0.1646	36.62%
Psychoticism	2	0.16	[−0.26, 0.59]	0.75	0.4522	Q(1) = 0.45	0.5007	0.00%

et al., 2007).

Overall previous research indicates similar patterns of personality in different mental disorders including other affective disorders (Kotov et al., 2010), anxiety disorders (Kotov et al., 2010), posttraumatic stress disorder (Kotov et al., 2010), substance use disorders (Kotov et al., 2010; Ruiz et al., 2008) and SCZ (Ohi et al., 2016). Especially meta-analyses by Kotov et al. and by Ohi et al. indicate large positive effect sizes for N and negative effect sizes for C and E (Kotov et al., 2010; Ohi et al., 2016). In conclusion, the personality profile of patients with BD we found in our meta-analysis (higher neuroticism, lower conscientiousness and lower extraversion than HC) is clearly not specific for the diagnosis of BD.

In contrast to our analysis, both meta-analyses found significant results for A and O. Kotov et al. found medium negative effect sizes for A and O for few of their investigated disorders, while Ohi et al. found medium negative effect size for A and small negative effect size for O of patients with SCZ (Kotov et al., 2010; Ohi et al., 2016).

Overall, some differences in methods between meta-analysis of Kotov et al. and our analysis should be noted. Kotov et al. included normative samples and data from general population samples in their control groups instead of focusing strictly on HC, thus we would expect smaller effect sizes compared to our analysis (Kotov et al., 2010). Contrary they found more extreme effect sizes for most of the personality traits than we evaluated in our analysis. For example they found large negative effect sizes for E (unspecified unipolar depression: $d = -0.92$ and dysthymic disorder: $d = -1.47$) and C (MDD: $d = -0.90$, unspecified unipolar depression: $d = -1.13$ and dysthymic disorder: $d = -1.24$), while we found small negative effect size for E ($d = -0.38$) and medium negative effect size for C ($d = -0.78$) (Kotov et al., 2010). This divergence in effect sizes might be driven by other underlying factors, which were not assessed in our analysis. Further, Kotov et al. defined a CI of 80% whereas we set a 95% CI for our analysis (Kotov et al., 2010). This difference might explain significant results for A and O for some of their investigated disorders, as in use of 95% CI these results might not have been significant.

In general, the similarities in expression of personality profiles across various disorders might support a transdiagnostic view on mental disorders. There is high comorbidity among mental disorders and symptoms overlap between different diagnostic categories which suggests that many psychiatric disorders can be characterized by shared underlying traits. As an example, psychiatric disorders might be described by an internalizing (emotions like sadness and anxiety) and an externalizing factor (impulsiveness, aggressiveness or rule breaking) (Eaton et al., 2015; Krueger and Eaton, 2015). Both of these factors were found to correlate with different personality traits (Griffith et al., 2010; Krueger et al., 2007; Krueger and Markon, 2006; Tackett et al., 2014). The Hierarchical Taxonomy Of Psychopathology (HiTOP) model goes further by uniting co-occurring syndromes into spectra and constructing psychiatric syndromes based on comorbid symptoms (Kotov et al., 2021, 2017). They describe correlations between clinical groups of disorders (internalizing, thought disorders and externalizing) and personality dimensions (negative affectivity, psychoticism, disinhibition and antagonism) (Kotov et al., 2021, 2017). These personality dimensions may be

understood as maladaptive versions of the FFM traits, as negative affectivity correlates with N, disinhibition with low C, detachment with low E and antagonism with low A (Krueger and Markon, 2014).

In line with the transdiagnostic view on psychiatric disorders, a recent meta-analysis of genetic risk loci, identified by genome-wide association studies (GWAS), indicates strong overlap between BD and several other disorders. Strongest associations were found between BD and SCZ ($r = 0.70$) followed by MDD ($r = 0.36$), OCD ($r = 0.31$) and anorexia nervosa ($r = 0.21$) (Lee et al., 2019, 2013). GWAS by Stahl et al. indicated genetic correlations between BD I and SCZ and BD II and MDD (Stahl et al., 2019). Further, Luciano et al. found various gene loci associated with N in a GWAS. They identified significant genetic correlations between N and depressive symptoms ($r = 0.82$, standard error (s.e.) = 0.03), subjective well being ($r = -0.68$, s.e. = 0.03) and MDD ($r = 0.69$, s.e.=0.07) (Luciano et al., 2017). These findings might provide the basis for analogies in personality traits of patients with BD and patients with other mental disorders.

Our findings of increased N in BD that is non-specific for this disorder might be interpreted within the scope of recent work of Barlow et al. (2021). It is suggested that individuals develop sensitivity for specific events (triggers) through experiences in childhood. These triggers stimulate negative emotions and can lead to the development of trigger-specific emotional disorders in individuals with high N. However, individuals with similar experiences in early life, thus related triggers, but with lower N rather not develop these disorders, as they show healthier levels of emotional functioning (Barlow et al., 2021).

In general, our findings highlight the importance of a detailed understanding regarding the interplay between mental disorders and personality traits. Watson and Naragon-Gainey outline three potential causal associations between psychopathology and personality: (i) personality traits might cause certain mental disorders (vulnerability model) or may influence their expression and course (pathoplasty model), (ii) disorders might influence personality either permanently (scar model) or temporarily (complication model) or (iii) both mental disorders and personality might underlie the same continuum (spectrum model) or might have the same etiology (common-cause model) (Watson and Naragon-Gainey, 2014). There exists empirical support for all of these models (Clark et al., 1994; Fanous et al., 2007; Kendler and Gardner, 2011; Kotov et al., 2010; Watson et al., 2005).

Our results indicate that older samples showed smaller differences in N between patients with BD and HC. This finding might support the vulnerability model as younger patients with BD might show stronger expressions of N during the beginning of their disease. However further evidence from longitudinal studies is needed to support this hypothesis. As another possible explanation, it has to be noticed that even though personality traits have been found stable over a long period of lifetime (Cobb-Clark and Schurer, 2012; Conley, 1985; Rantanen et al., 2007), a meta-analysis by Roberts et al. showed a development of traits during lifetime in a non-clinical population (Roberts et al., 2006). Emotional stability, the opposite of N, has been suggested to increase with older age (Roberts et al., 2006), which indicates that N decreases over lifetime in nonclinical individuals. Additional findings suggest that patients with BD might not develop the same strong emotional stability than HC during lifetime, as individuals with BD seem to have impaired emotion regulation strategies with an important impact on functional outcome (Lima et al., 2018). Further, they were reported to feel less able to use adaptive emotion regulation strategies (Lima et al., 2018). Consequently, our finding of smaller differences of N between BD and HC in older samples might be driven by an natural development of personality traits combined with difficulties in emotion regulation strategies.

4.2. Limitations and future directions

This study has some limitations that should be considered when interpreting our results.

As mentioned above, we were not able to perform a subgroup analysis on the different mood states or different types of BD, as the number of studies that reported these data was limited. Thus, we could not evaluate if our results were driven by one of these factors. It remains to be determined whether expression of personality traits remains consistent in patients with BD during different mood states or varies with depression and mania.

In this context it should be noted that six different manuals of diagnostic criteria were used to identify patients with BD included in our analysis (Table 1). There are some taxonomic differences and small differences in diagnostic criteria between these. It should be noted that the modern diagnostic criteria tends to a categorial understanding of BD with depression and mania, whereas earlier recognition of BD was more spectrum orientated and thus might include subsyndromal or subtreshould patients (Mason et al., 2016). Aware of this we might expect a difference in expressions of personality traits. However, as discussed above, we found no moderating effect for the year of publication, suggesting that the various diagnostic manuals do not lead to significantly different results.

Moreover, our analysis was limited to the domain-level of personality traits. Due to the lack of available data on facets of each of the five domains, we were not able to perform analyses on specific subsets. Investigations into how specific facets correlate with BD and how mood states influence the correlation is an outstanding task for future research.

Our results represent a cross-sectional comparison of personality traits in BD and HC, allowing no conclusions on how personality traits might influence onset, course and outcome. In future research examining expressions of personality traits in longitudinal studies might indicate vulnerability for BD or might indicate a poor outcome due to BD should be of great significance, as they could have a great impact on prevention and treatment. Our results can provide the basis for these future investigations by identifying dominant traits that should be focused on.

Additionally, in this analysis we exclusively focused on BD. We discussed similarities with findings on differences in personality traits between other mental disorders and control groups, but were not able to compare these and our findings quantitatively, as criteria on measuring diagnosis and defining control groups were different. Future investigations could aim at a systematic comparison of personality traits of different mental disorders to identify tendencies in these differences.

4.3. Implications and conclusions

In conclusion, the results of our meta-analysis show significant differences between patients with BD and HC in three of the investigated personality traits (N, E and C). Patients with BD scored higher on N and lower on E and C. Additionally, differences in N levels were smaller the older the sample group was.

In this meta-analysis, we identified dominant expressions of personality traits in patients with BD. Our analysis (1) is the first meta-analysis comparing FFM personality scores of patients with BD and HC and thus emphasizes the importance of personality assessment in patients with BD. Our work (2) adds to prior research on personality in psychiatric disorders and thus contributes to form a foundation for future investigations on specific expressions of personality traits across different psychiatric diagnoses and moreover (3) for examining similarities in personality across transdiagnostic spectra. It further (4) provides the basis for future research with focus on onset, course and outcome of BD that might help to identify individuals at risk. All of these implications will have a great impact on transdiagnostic personality research and thereby on prevention and treatment of various psychiatric disorders.

Term	Definition
Conceptualization	Ideas; formulation or evolution of overarching research goals and aims

(continued on next page)

(*continued*)

Methodology	Development or design of methodology; creation of models
Software	Programming, software development; designing computer programs; implementation of the computer code and supporting algorithms; testing of existing code components
Validation	Verification, whether as a part of the activity or separate, of the overall replication/ reproducibility of results/ experiments and other research outputs
Formal analysis	Application of statistical, mathematical, computational, or other formal techniques to analyze or synthesize study data
Investigation	Conducting a research and investigation process, specifically performing the experiments, or data/evidence collection
Resources	Provision of study materials, reagents, materials, patients, laboratory samples, animals, instrumentation, computing resources, or other analysis tools
Data Curation	Management activities to annotate (produce metadata), scrub data and maintain research data (including software code, where it is necessary for interpreting the data itself) for initial use and later reuse
Writing - Original Draft	Preparation, creation and/or presentation of the published work, specifically writing the initial draft (including substantive translation)
Writing - Review & Editing	Preparation, creation and/or presentation of the published work by those from the original research group, specifically critical review, commentary or revision – including pre-or postpublication stages
Visualization	Preparation, creation and/or presentation of the published work, specifically visualization/ data presentation
Supervision	Oversight and leadership responsibility for the research activity planning and execution, including mentorship external to the core team
Project administration	Management and coordination responsibility for the research activity planning and execution
Funding acquisition	Acquisition of the financial support for the project leading to this publication

Role of funding source

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CRediT authorship contribution statement

Natalie Hanke: Conceptualization, Software, Formal analysis, Investigation, Data curation, Writing – original draft, Visualization. **Nora Penzel:** Conceptualization, Methodology, Validation, Data curation, Writing – original draft, Visualization. **Linda T. Betz:** Conceptualization, Methodology, Software, Validation, Formal analysis, Data curation, Writing – original draft, Visualization. **Melanie Rohde:** Writing – original draft. **Lana Kambeitz-Ilankovic:** Writing – original draft. **Joseph Kambeitz:** Conceptualization, Writing – original draft, Visualization, Project administration, Funding acquisition.

Declaration of competing Interest

None.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2022.01.067.

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4 Discussion

4.1 Findings and Context

This project aimed to contrast and compare personality traits as defined by the FFM and the TFM, in individuals with BD and HC.[1] We analyzed 18 studies encompassing 1694 individuals with BD and 2153 HCs, discovering considerable distinctions in personality traits between the two groups. Of the examined personality traits, three showed significant differences (N, C, and E). As hypothesized, individuals with BD showed elevated N levels (large positive effect size) and reduced E levels (small negative effect size) compared to HC. Further, patients scored lower on C than HC (medium negative effect size). In addition, our findings indicated that age had moderating impact on the effect size of N: the older the sample group, the smaller the differences in N scores between BD and HC. Essentially, these results were robust and resilient to potential publication bias and confounding variables like study quality and years of publication.[1]

Our meta-analysis showed significant positive effect size for N, comparing BD and HC, echoing the findings of previous studies.[1,42-48] Overall, elevated levels of N have been linked to negative emotional experiences, correlating with various negative emotions like fear/anger, guilt/dissatisfaction and anxiety.[1,59-62] Unexpectedly, different research groups have found that high N levels in BD are associated not only with depression, but with all dimensions of bipolar symptoms: including both depressive [1,19,63,64] and manic symptoms.[1,64] The hypotheses of Murray et al. might provide insight into the interrelation between N and BD.[1,26] They outline the similarities between N and BD in terms of instability in behavior, mood and cognitive processes as they are elementary parts of both N[65-67] and BD.[1,68,69]

Additionally, our analysis also revealed a small negative effect size for E. The individual results of the studies included in our meta-analysis reported reduced levels of E compared with HC,[43,47,53,54] or no significant difference.[1,48,52] Studies have suggested that the impact of E may vary across different mood states of BD. They indicate that BD patients in a depressed mood exhibit low levels of E, whereas those in a manic state display high levels of E.[1,25,64] Unfortunately, our analysis did not have the necessary data to differentiate between specific mood states, thus our results

cannot be attributed to a specific mood state.[1] In addition, the correlation between BD and facets of E can vary. According to Watson et al., there is a positive association between mania symptoms and extraversion facets excitement seeking and venturesomeness.[1,70] In the present meta-analysis a more detailed synthesis was not possible, as available data was restricted on the various facets of personality traits.[1]

Additionally, our meta-analysis uncovered a medium negative effect size for C. Several included studies described that individuals with BD have lower C levels than HC, [47,54] whereas another study found no significant discrepancy between individuals with BD and HC.[1,55] Low C levels not only have a significant impact on mental health, but also on physical health. Studies have linked low C levels with behaviors that negatively impact physical health, making it a major predictor of mortality.[1,71,72]

Overall, prior research suggests similar personality patterns across several mental disorders, including other mood disorders,[50] substance use disorders,[50,73] posttraumatic stress disorder,[50] anxiety disorders,[50] and SCZ.[1,51] In particular, meta-analyses by Kotov et al. and Ohi et al. reveal substantial positive effect sizes for N and negative effect sizes for C and E. [1,50,51] In summary, the expression of personality traits we observed in our analysis, including higher N, lower C and lower E in BD individuals compared to HC, are nonspecific to a BD diagnosis.[1] Contrary to our results, both meta-analyses discovered significant findings for A and O. Ohi et al. reported a medium negative effect size for A and a small negative effect size for O in SCZ, whereas Kotov et al. identified for some of their examined disorders medium negative effect sizes for O and A.[1,50,51] Moreover, it's important to note some methodological differences between the meta-analysis of Kotov et al. and our analysis. Kotov et al. utilized normative samples and general population data in their control groups, rather than solely HC, so we would anticipate smaller effect sizes in comparison to our work.[1,50] In contrast, they evaluated for many personality traits more extreme effect sizes than we found in our work. For instance, they detected large negative effect sizes for C (MDD: d = -0.90, unspecified unipolar depression: d = -1.13 and dysthymic disorder: d = -1.24) and E (unspecified unipolar depression: d = -0.92 and dysthymic disorder: d = -1.47), whereas our findings indicated medium negative effect size for C (d = -0.78) and small negative effect size for E (d = -0.38).[1,50] This difference in effect sizes could be due to additional underlying factors that were not evaluated in our work.[1] Additionally, it should be noted that Kotov et al. employed a CI of 80%, while we utilized a CI of 95% in our work. This divergence could potentially account for the significant results of A and O

for certain examined illnesses, given that these results might not have been significant if 95% CI had been used.[1,50]

Overall, the resemblances in the manifestation of personality traits across disorders may lend support to a transdiagnostic perspective on mental illnesses. Overlap of symptoms between different diagnostic categories and strong comorbidity among mental disorders, suggest that numerous psychiatric illnesses can be defined by shared underlying features. For instance, mental disorders can be characterized by an externalizing factor (impulsivity, aggressiveness or rule breaking) and an internalizing factor (emotions such as sadness and anxiety).[1,74,75] Previous research has identified correlation between these two factors and various personality traits.[1,76-79] The Hierarchical Taxonomy Of Psychopathology (HiTOP) model takes this idea further by grouping concurrent syndromes into spectra and outline psychiatric syndromes based on overlapping symptoms. In this model, clinical groups of mental disorders (externalizing, internalizing and thought disorders) are correlated with personality characteristics (psychoticism, negative affectivity, antagonism and disinhibition). [1,80,81] These dimensions can be seen as opposite versions of the FFM traits, while detachment is correlated with low E, negative affectivity with N, antagonism with low A and disinhibition with low C.[1,82]

Supporting the transdiagnostic perspective of psychiatric illnesses, a recent meta-analysis that identified genetic risk loci through genome-wide association studies (GWAS), suggests great similarities between BD and various other mental disorders. Greatest correlations were shown between BD and SCZ (r = 0.70). Further correlations in descending order were BD and MDD (r = 0.36), OCD (r = 0.31), and anorexia nervosa (r = 0.21).[1,83,84] GWAS by Stahl et al. found genetic associations within BD I and SCZ as well as between BD II and MDD.[1,85] In addition, Luciano et al. evaluated in a GWAS several gene loci associated with N and determined significant genetic correlations connecting N and depressive symptoms (r = 0.82, standard error (s.e.) = 0.03), MDD (r = 0.69, s.e. = 0.07) and subjective well-being (r = -0.68, s.e. = 0.03).[1,86] These findings suggest that the similarities in personality traits between individuals with BD and those with other psychiatric disorders may be based on shared genetic associations.[1]

The elevated N levels we found in BD, which are not specific to this disorder, could be explained in the context of recent research by Barlow et al.. They suggest that people develop sensitivity to certain events (triggers) based on childhood

experiences. These triggers arouse negative emotions that might cause the genesis of trigger-specific “emotional disorders” in subjects which showed elevated N levels. Although, individuals who have similar early life experiences, hence associated triggers, but show lower N are less likely develop these illneses, as they display better emotional functioning. This suggests that N levels could be a shared risk factor across various mental disorders, including BD.[1,87]

Overall, the results of our analysis emphasize the crucial significance of a detailed comprehension of the interaction between mental disorders and personality traits. Watson and Naragon-Gainey have identified three possible causal correlations between psychopathology and personality: (i) *vulnerability model*: personality traits may cause specific mental illnesses or *pathoplastiy model:* affect their manifestation and progression, (ii) *scar model:* disorders might cause a permanent effect on personality or *complication model:* have a temporary impact, or (iii) *spectrum model:* mental disorders and personality traits may be located on the same continuum or *common-cause model:* might have the same etiology.[1,61] There is empirical evidence for all of these models.[1,50,88-91]

Based on our findings, it appears that older samples exhibit fewer discrepancies in N levels between patients with BD and HC. This result could sustain the vulnerability model, which proposes that younger individuals with BD may exhibit more pronounced N expressions than HC at the onset of their illness. Nevertheless, more comprehensive data from longitudinal investigations is necessary to substantiate this hypothesis. An alternate explanation could be that although personality traits are typically shown to be stable throughout lifetime,[39-41] meta-analysis by Roberts et al. indicated trait evolution during lifetime in a nonclinical population.[1,92] Furthermore, emotional stability, which is the reverse of N, has been found to grow over lifetime,[92] suggesting that N levels might reduce with older age in nonclinical individuals.[1] Further results indicate that individuals with BD may not experience the same degree of emotional stability as HC throughout their lifespan, as patients with BD appear to show impaired emotion regulation techniques that can have a significant impact on their functional outcomes. Additionally, these individuals were described to feel less capable of utilizing effective emotion regulation strategies. [1,93] Therefore, our results regarding reduced discrepancies in N levels between BD and HC in older samples may be attributable to the natural evolution of personality traits combined with problems in implementing effective emotion regulation strategies.[1]

4.2 Limitations and future directions

There are certain limitations to this meta-analysis that should be taken into account while interpreting our findings.

As mentioned previously, a subgroup analysis of various types of BD or different mood states was not feasible due to the limited number of studies that reported this information. Therefore, we were unable to assess whether our findings were influenced by any of these factors. It still needs to be investigated whether the manifestation of personality traits in individuals with BD remains consistent across various mood states or whether it differs between depression and mania.[1]

In this respect, it should be perceived that our analysis incorporated six different diagnostic criteria to determine the individuals with BD. There are small discrepancies in diagnostic criteria and some taxonomic variances between those. Further, it is worth noting that the earlier understanding of BD was more focused on the spectrum, which may have resulted in the inclusion of subsyndromal or subthreshold patients. However, modern diagnostic criteria tend to towards a categorical approach towards BD, considering depression and mania.[1,94] Considering the aforementioned factors, it is reasonable to expect a difference in the manifestation of personality traits. However, as mentioned previously, our moderator analysis did not indicate any effect for year of publication, which implies that the diverse diagnostic manuals employed in our analysis did not significantly impact our findings.[1]

Further, our meta-analysis was restricted to the domain-level of personality traits. We were unable to conduct an analysis on specific facets of the six domains due to the lack of available data. Investigating how individual subsets relate to BD and how mood states influence these associations is a pending task for future research.[1]

It is important to note that our results are derived from a cross-sectional investigation of personality traits in individuals with BD and HC. Therefore, our findings do not provide insight into how personality traits may impact the onset, progression, or outcome of the disorder.[1]

In future studies, it would be crucial to investigate the manifestation of personality traits in longitudinal designs, which may provide insight into the predisposition to BD or poor outcomes related to the disorder. Such investigations could have significant

implications for prevention and treatment strategies. Our findings may serve as a foundation for future research by exposing the dominant personality traits that should be prioritized for further examination.[1]

In addition, we focused solely on BD in this analysis. We evaluated resemblances with results on distinctions in personality traits between other psychiatric disorders and control groups. However, we were unable to perform a quantitative comparison between our results and those of other mental disorders and control groups, as the criteria used to measure diagnosis and define control groups varied across studies. Future studies could aim to systematically compare expression of personality traits across various mental disorders to determine leanings in these differences. Such investigations could provide valuable insights into the underlying mechanisms and potential treatment targets across psychiatric disorders. .[1]

4.3 Implications and Conclusions

Concluding, our meta-analysis indicates that patients with BD differ significantly from HC in three of the evaluated personality traits (N, E, and C), with BD patients scoring higher on N and lower on E and C. Furthermore, the age of the sample group was found to be a moderator of the N difference, with smaller differences observed in older samples.[1]

Our meta-analysis uncovered prominent expressions of personality traits among individuals with BD. This analysis (i) is the primary meta-analysis to contrast TFM/FFM personality levels of individuals with BD and HC, emphasizing the importance of personality assessment in individuals with BD. Our work (ii) complements previous literature on personality in mental disorders and helps to establish a basis for further exploration of particular expressions of personality traits in various mental disorders and moreover (iii) for investigating resemblances in personality across transdiagnostic spectra. In addition, (iv) our analysis offers a foundation for future investigations focusing on the onset, course and outcome of BD and thus could help to identify individuals at risk.[1]

The various implications of our findings highlight the importance of further transdiagnostic personality investigations and understanding their potential impact on the prevention and treatment of diverse mental disorders. This emphasizes the need

for future research to focus on specific expressions of personality traits across various psychiatric diagnoses, which could help identify individuals at risk and inform personalized treatment approaches. Overall, our study contributes to the growing body of literature on personality in psychiatric disorders and highlights the importance of personality assessment in patients with BD.[1]

5 References

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