

Comorbidity bipolar disorder and personality disorders

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Abstract

BACKGROUND: Outcome in bipolar patients can be affected by comorbidity of other psychiatric disorders. Comorbid personality disorders are frequent and may complicate the course of bipolar illness. We have much information about treating patients with uncomplicated bipolar disorder (BD) but much less knowledge about possibilities for patients with the comorbidity of BD and personality disorder.

METHOD: We conducted a series of literature searches using, as key words or as items in indexed fields, bipolar disorder and personality disorder or personality traits. Articles were obtained by searching MEDLINE from 1970 to 2012. In addition, we used other papers cited in articles from these searches, or cited in articles used in our own work.

RESULTS: Tests of personality traits indicated that euthymic bipolar patients have higher scores on harm avoidance, reward dependence, and novelty seeking than controls. Elevation of novelty seeking in bipolar patients is associated with substance abuse comorbidity.

CONCLUSION: Comorbidity with personality disorders in BD patients is associated with a more difficult course of illness (such as longer episodes, shorter time euthymic, and earlier age at onset) and an increase in comorbid substance abuse, suicidality and aggression. These problems are particularly pronounced in comorbidity with borderline personality disorder. Comorbidity with antisocial personality disorder elicits a similar spectrum of difficulties; some of the antisocial behavior exhibited by patients with this comorbidity is mediated by increased impulsivity.

INTRODUCTION

The term “bipolar disorder” (BD) is the contemporary diagnosis used for what was widely known as manic depressive illness. Two types are now recognized in classification, bipolar disorder type I and type II (BD I and BD II). Both types con-

stitute highly disabling conditions. BD I, BD II, and subthreshold hypomania comprise the bipolar spectrum (Merikangas & Lamers 2012). Household interviews of 61,392 community adults in 11 countries have established aggregate lifetime prevalence of 0.6% for BD I, 0.4% for BD II, and 2.4% for bipolar spectrum (Merikangas 2012).

Treatment targets are the resolution of symptoms, the restoration of psychosocial functioning and the prevention of relapses. Pharmacotherapy constitutes essential mental health care in BD, but important parts of comprehensive treatment are specific forms of psychotherapy. To date, several papers about treatment guidelines for BD have been published (APA 2002; Goodwin 2003; Grunze *et al.* 2002, 2003, 2004; O'Dowd 2006; Yatham *et al.* 2005, 2006). There is also a number of guideline documents developed by national bodies that have been published. The CANMAT (Yatham *et al.* 2006) and the NICE (O'Dowd 2006) guidelines are the most recent ones.

Comorbidity with other psychiatric disorders modify outcome of bipolar disorder. We would like to concentrate our attention on frequency of comorbid personality disorders which can to complicate the course of bipolar disorder illness. Our knowledges about managing uncomplicated bipolar disorder are wide, but we don't know so much about treatment possibilities for bipolar patients with the comorbidity of personality disorder.

The definition of the term "comorbidity" is currently in flux. Its original meaning was to indicate the presence of more than one illness or disorder in an individual at the same time. However, it has become clear that it may be difficult to determine whether two concomitant diagnoses indicate the presence of two clearly defined clinical entities, or reflect multiple manifestations of the same entity. From that perspective, it would be inaccurate to say that a comorbidity complicates the course of illness. It is also possible to see comorbidity as the presence of one illness with an elevated risk for another illness in an individual. Most authors, including ourselves, use the term its original meaning; the reader should keep in mind other possibilities.

METHOD

Using by key words or indexed fields: bipolar disorder, personality disorder, and personality traits we explored a series of literature. Articles were obtained by searching MEDLINE from 1970 (its establishing) to 2012. In addition, we used other papers cited in articles from these searches, or cited in articles used in our own work. Articles were selected for inclusion based on the following considerations: numbers of studied patients, using of diagnostic criteria, sequencing of disorders, and validated methods of assessment.

BIPOLAR DISORDER AND PERSONALITY TRAITS

An individual's personality develops early, is stable, and has a strong heritable component. Personality traits can be understood as one of the factors which influence the predisposition to BD and may help to distinguish between major depressive disorder (MDD), BD I, and BD II. Personality traits are also being considered as

potentially useful endophenotypes for the investigation of the genetic basis of complex mental disorders (Savitz & Ramesar 2006). Most studies of specific personality traits of patients with bipolar disorder have sought to differentiate these patients from normal controls (Nowakowska *et al.* 2005; Strong *et al.* 2007) or to differentiate bipolar from unipolar patients (Bagby *et al.* 1997; Bagby *et al.* 1996; Jain *et al.* 1999).

Cloninger's psychobiological model is one of the personality theory which demonstrates strong heritability by using the temperament and character inventory (TCI). Cloninger's psychobiological model suggests four parts of personality that are automatic, innate and partly hereditary reactions to external stimuli (Cloninger 1987) According Cloninger's model, temperament consists of four parts: reward dependence (RD), novelty seeking (NS), persistence (P) and harm avoidance (HA). In addition, Cloninger's model (1993) includes three factors of character: self-transcendence, cooperativeness, and self-transcendence.

Initial studies with bipolar adults used the Tridimensional Personality Questionnaire (TPQ) (Bagby *et al.* 1992), a forerunner to the Temperament and Character Inventory (TCI) (Cloninger *et al.* 1994). An outpatient sample of euthymic bipolar patients had significantly higher TPQ scores on NS and HA scores versus healthy subjects (Young *et al.* 1995). This study also compared the euthymic bipolar subjects to recovered unipolar depressed subjects and found that the two groups did not differ on HA; however, NS scores were elevated in subjects with bipolar compared with unipolar patients.

In a sample of hospitalized adults, bipolar patients had significantly higher NS and RD compared to unipolar depressed patients whereas the unipolar subjects were higher on HA (Janowsky *et al.* 1999). However, bipolar subjects who were depressed were equivalent in HA compared to unipolar depressed subjects, but still scored higher on NS and RD.

In a study of patients with first-episode mania, higher TPQ NS dimensional scores at the time of hospital discharge were associated with a failure to reach functional recovery at 6 months follow up (Strakowski *et al.* 1993). Studies using the TCI in bipolar adults found they were significantly higher on the temperament dimensions of HA and RD in comparison to healthy control subjects (Engstrom *et al.* 2004). These findings were not replicated by Sayin *et al.* (2007) in a Turkish bipolar sample. This study found no difference in TCI temperament scores, but noted that bipolar subjects had lower scores on the self-directedness and cooperativeness domains compared to healthy controls. Higher NS on the TCI was also seen in bipolar subjects with current substance abuse compared to bipolar subjects with remitted substance abuse and bipolar subjects without a history of substance abuse (Haro *et al.* 2007).

Bipolar patients (n=277) completed the TCI questionnaire also in another study (Harley *et al.* 2012) and then were also asked about their lifetime psychiatric

diagnoses. All investigated subjects were divided into four groups (BD I, BD II, MDD, and nonaffected relatives), and were compared. Total harm avoidance was higher in both major depressive disorder and both bipolar groups than in the unaffected relatives. However, the mood disorder groups did not differ among themselves. Patients suffering from major depressive disorder and unaffected relatives had lower self-transcendence than patients suffering from BD I. Harm avoidance may reflect a trait marker of mood disorders whereas high self-transcendence can be specific to bipolar disorder, whereas harm avoidance seems to be trait marker of mood disorder. As self-transcendence is partly heritable, genes that affect self-transcendence may be of relevance for vulnerability to bipolar disorder.

Studies employing the Temperament and Character Inventory (TCI) or the Tridimensional Personality Questionnaire (TPQ) reported that patients with BD showed higher scores on Harm avoidance than did controls. (Nowakowska *et al.* 2005; Blairy *et al.* 2000; Engstrom *et al.* 2004; Loftus *et al.* 2008; Strober & Carlson 1982; Young *et al.* 1995; Nery *et al.* 2008).

Studies using the NEO Personality Inventory (NEO-PI) to assess personality traits revealed that patients with BD had significantly higher Neuroticism scores in comparison with normal controls (Nowakowska *et al.* 2005; Strong *et al.* 2007). Revised NEO (NEO-PI-R) was used in a study (Kim *et al.* 2012) that included 47 women and 38 men suffering from BD I and 23 women and 20 men suffering from BD II. All patients were in remission for at least 8 weeks prior to study entry. Patients suffering from BD II scored higher than BD I patients on Neuroticism dimension and its four components (Anxiety, Depression, Self-consciousness, and Vulnerability). On the other hand, BD II patients scored lower than BD I patients on the Extraversion dimension and its components: Positive emotion. Competence and Achievement-striving, Conscientiousness component was, surprisingly, significantly lower for BD II than for BD I patients. There were no significant between-group differences in the Openness and Agreeableness components. One earlier study described the distinct temperamental profiles of BD I and BD II patients using various temperament and personality scales, but excluding the NEO-PI (Akiskal *et al.* 2006).

Results of studies suggest that bipolar patients in remission suffer from higher neuroticism than normal controls and BD II patients suffer more than BD I patients. Moreover BD I patients tend to feel positive emotions in their euthymic states.

COMORBIDITIES IN BIPOLAR DISORDER

The diagnosis and treatment of bipolar disorder are often complicated by comorbidity. According Vieta *et al.* (2001) rates of lifetime psychiatric comorbidity in bipolar I samples range from 50% to 70%. Comorbidity worsens course and prognosis of illness (McElroy

2004). Comorbidity means the occurrence of two disorders in the same patient. According to Krishnan (2005) psychiatric comorbidity is often associated with earlier onset of bipolar disorder, with more severe course, contributes to poorer treatment adherence, worse outcomes, namely increases risky of suicide leads to further complications. Familial comorbidity may be caused by genetic linkage or shared environmental exposures. Relatives of a patient suffering from one disorder tend to have the comorbid disorder than individuals in a family not affected by either disorder (McElroy *et al.* 2001).

COMORBIDITY OF BIPOLAR DISORDER AND PERSONALITY DISORDERS

Course of bipolar disorder can be complicated by personality disorders. Patients with bipolar disorder suffer from comorbid personality disorders in more than 36% (Vieta *et al.* 2001; Kay *et al.* 2002; Brieger *et al.* 2003). The odd/eccentric personality disorders are less frequent than dramatic/emotionally erratic and fearful/avoidant personality disorders (George *et al.* 2003).

Kay *et al.* (2002) studied 52 euthymic male bipolar subjects. Authors concluded that the cluster A and cluster B disorders are the most frequent. According other studies (George *et al.* 2003; Altindag *et al.* 2006) the cluster A is less common than cluster B or C in bipolar patients.

As argued by Hirschfeld *et al.* (1986), comorbid personality disorder observed in bipolar patients may be also a consequence of the bipolar illness, which may affect personality by decreasing the emotional strength and favoring anancastic, anxious, and paranoid aspects of the patient's personality traits.

Bipolar disorder and comorbid personality disorder create poorer outcome and may leads to worse psychosocial adjustment (Colom *et al.* 2000), also leads to higher number of affective episodes (Vieta *et al.* 2001). Perugi and Akiskal (2002) claims that the problem may be to distinguish mood cycling within BD II from cyclothymic temperament or borderline personality disorders in sometimes.

Kay *et al.* (1999) suggested that cluster A diagnoses are more common in the bipolar patients with alcohol problems. History of comorbid alcohol use disorder in patients suffering from bipolar patients is connected with personality disorder based on the SCID II compared with bipolar patients without history of alcohol abuse (Winokur *et al.* 1995).

Personality features are important in predicting outcome of bipolar disorder, how suggest studies. Poor compliance disorders is strongly associated with personal comorbidity (Colom *et al.* 2000). Cluster B and cluster C personality disorders are more common than cluster A (George *et al.* 2003) in bipolar patients. Patients suffering from borderline personality disorder often do not exhibit clinically expressed symptoms of bipolarity (Deltito *et al.* 2001). Bipolar patients with co-

occurring personality disorder are less likely to achieve recovery and tend to experience residual mood symptoms during remission). Comorbid bipolar patients also show a higher number of mixed features, depressive episodes, and suicide attempts (Vieta *et al.* 2001; Dunayevich *et al.* 2000; George *et al.* 2003).

Rossi *et al.* (2001) and Vieta *et al.* (2001) concluded that narcissistic personality, borderline personality disorder and obsessive-compulsive personality disorder are more frequent in bipolar patients. Avoidant personality disorder is more prevalent among unipolar depressive patients Brieger *et al.* (2003). In accordance with them Hirschfeld *et al.* (1986) claimed that, bipolar affective disorder may determine a lower level of emotional strength and higher levels of introversion.

Borderline personality disorder (BPD) is disorder which typical characteristics as unstable and rapidly changing mood poor or lost of self control and , impulsivity (WHO 1992). These characteristics can be also observed in bipolar disorder. The high co-occurrence of both disorders brought some suggestions that borderline personality disorder should be understood as part of an affective spectrum (Sjastad *et al.* 2012).

Borderline personality disorder appears to involve affective lability, which can affect the effectiveness of known treatments for bipolar spectrum disorders (Deltito *et al.* 2001) Deltito *et al.* (2001) found that 45% of patients with BPD had a co-occurring bipolar affective disorder.

According Paris (2007), bipolar disorder and borderline personality disorder may share biological basis. Other researchers promote idea that the comorbidity BPD and bipolar disorders is not more specific than for other personality disorders; for example McGlashan *et al.* (2000) did not find significant differences when comparing patients with borderline personality to avoidant, schizotypal, or obsessive-compulsive types, with regard to presence of bipolar disorder. Next authors enforce idea that borderline persons have qualitatively different mood swings than bipolar patients (Henry *et al.* 2001), and moreover symptoms do not respond willingly to mood stabilizers (Paris 2010). Mentioned studies support the theory of BPD as an independent disorder and it could be understood like separate and, qualitatively different disorder

Nevertheless, it has been suggested that borderline personality disorder and mood disorders, including bipolar disorders, are co-transmitted in families (Henry *et al.* 2001). In contrast, Stone (2006) understands patients in whom borderline personality disorder and bipolar disorder co-occur as representing an interaction of biological and environmental forces. Premorbid personality associated with BD II is characterized as the reward-dependent, passive-avoidant/dependent tendency of personality (Takata & Takaoka 2000).

Cluster B personality disorder (usually borderline) was associated with poor outcome after a manic episode (Dunayevich *et al.* 2000), higher incidence of suicide attempts (Garno *et al.* 2005, Leverich *et al.* 2003) and

a 'difficult' course of illness (Kay *et al.* 2002). In bipolar disorder, Anti-Social Personality Disorder (ASPD) predicted severe course of illness, presence of substance-use disorder, and suicidal behavior (Swann 2011).

As concluded some investigators, borderline personality patients suffered more from unipolar than bipolar disorders In study (Sjastad *et al.* (2013) borderline personality patients had lower rate of depression than other personality disorder groups (for example paranoid or histrionic). However the rate of bipolar disorder tended to be higher in borderline personality persons. The results above mentioned study suggest that borderline personality disorder has a closer connection to bipolar affective disorders than disorders in the unipolar spectrum. This association may have reasons in etiological bases or in some similar overlapping diagnostic criteria.

Neurobiological study (Koenigsberg 2010) suggests that affective instability in borderline personality disorder is caused by reactivity to psychosocial trauma, while affective instability in bipolar disorder is endogenous / internal. Wilson *et al.* (2007) claims that bipolar patients with comorbid BPD tend to higher rates of cognitive impairments than bipolar patients those who are BPD free. It was found that while affective instability is characteristic for both BPD and bipolar disorder, only BPD is associated with impulsivity (Benazzi 2006). As claims Lewis *et al.* (2009), impulsivity is typical for mania, but it is only the state in manic episode and it is not trait marker of bipolar disorder. Moreover increasing impulsivity among bipolar patients in euthymic period was not found. Maybe, impulsivity differentiates BPD from bipolar disorder. Coulston *et al.* (2012) reported that rapid cycling bipolar disorder and BPD had more overlapping phenomenological and etiological features than BD I and BD II. It is necessary to do further research in this area.

Impulsive behavior, increased incarceration or arrest, addictive disorders and suicidal behavior are characteristic for both: ASPD and BD. In case of combined disorders these characteristics appear more severe. Patients prone to higher rates of addictive disorders, suicidal behavior and are more impulsive (Swann 2011). In addition those patients have earlier onset of bipolar disorder with a more recurrent and predominately manic episodes, those patients tend to be more impulsive.

Results of some family aggregation studies have suggested existence of certain common mechanisms for bipolar disorder, substance-use disorders and cluster B personality disorders. Nurnberger *et al.* (2004) found an aggregation of ASPD, drug dependence, anxiety disorders and mood disorders. Similarly Zanarini *et al.* (2009) found extensive co-aggregation among borderline personality disorder, other cluster B personality disorders, affective disorders, and substance-use disorders, suggesting common familial factors, particularly in the areas of affective disturbance and impulsivity.

Studies focusing primarily on BD and ASPD and conduct disorder (CD) have suggested a greater speci-

ficity. Comparing relatives of children with CD and/or bipolar disorder to controls, Wozniak *et al.* (2001) found high rates of CD/ASPD and bipolar disorder in relatives of children with combined CD and bipolar disorder. The combination of CD/ASPD and bipolar disorder was found exclusively among relatives of children with combined disorders and not in those with CD or bipolar disorder alone, suggesting that CD/ASPD and bipolar disorder represent separate disorders, and that “the combination of CD and bipolar disorder may be a distinct nosological entity”. Similarly, a blinded, controlled family study using structured diagnostic interviews of 157 children with bipolar I disorder (487 first-degree relatives), 162 having Attention Deficit Hyperactivity Disorder (ADHD) without bipolar I disorder (511 first-degree relatives) and 136 healthy controls (411 first-degree relatives) found that relatives of children with bipolar I disorder had high rates of ASPD compared with relatives of controls, but the effect lost significance after correcting for the presence of CD/ASPD in the probands (Wozniak *et al.* 2010).

Therefore, family studies suggest that bipolar and ASPD may be disorders sharing common characteristics (e.g., impulsivity), that bipolar disorder and ASPD may be disorders with different mechanisms for similar symptoms and that the apparent combination of bipolar disorder and ASPD may be an independent disorder.

Mechanisms predisposing to impulsivity could cut across bipolar disorder and ASPD, or disorder-specific mechanisms could interact, contributing to behavioral complications of combined bipolar and personality disorders (Mezzich *et al.* 2007).

In bipolar disorder, comorbid ASPD was associated with a history of suicide attempts, addictive disorders and many episodes (Swann *et al.* 2010).

FAMILIAR AND GENETIC PATTERNS

Genes strongly influence the occurrence of bipolar disorder (see Shih *et al.* 2004 for a review). First-degree relatives of both schizophrenic and psychotic bipolar individuals show increased schizotypal and conceptual disorganization as measured by the Schizotypal Personality Questionnaire (SPQ) (Raine 1991), in contrast to scores of first-degree relatives of non-psychotic bipolar individuals (Schurhoff *et al.* 2005). Hyperthymic temperament (i.e., affective lability, cognitive dysregulation, identity problems, insecure attachment, and self-harm) has been shown to be elevated in first-degree relatives of bipolar patients (Kesebir *et al.* 2005). These features are broadly consistent with the clinical symptoms of bipolar disorder (Pukrop *et al.* 2001).

IMPACT ON TREATMENT

It is evident that course of bipolar disorder and its treatment are affected by comorbid personality disorder. It includes poorer overall outcome (Garno *et al.* 2005)

high rates of suicidality (Henry *et al.* 2001, depression onset (Tohen *et al.* 2003), and less favorable response to lithium (Sasson *et al.* 2003). Bipolar patients with comorbid personality disorder had greater severity of residual mood symptoms than patients of comorbidity free. The presence of a personality disorder in euthymic bipolar patients leads to a more difficult course, lower level of employment, consumption of more psychiatric medications, and brings alcohol and substance abuse problems. (Kay *et al.* 2002).

Therapeutic implications may have the overlap between bipolar disorder and borderline personality. In a retrospective study Preston *et al.* (2004). Criteria for borderline personality disorder met 40% subjects. Patients with comorbid personality disorder had a more frequent history of substance abuse and symptoms of ADHD in childhood. Treatment by lamotrigine was successful in both groups, lamotrigine alleviated borderline symptoms and also bipolar symptoms.

Similarly results brought a double-blind placebo-controlled pilot study (Frankenburg & Zanarini 2002). On based of results authors suggest that divalproate can be safe and effective in the treatment of women with comorbid borderline personality disorder and BD II. Divalproate decreased impulsivity, irritability, anger, and aggression It would be useful to remind that it is best not to diagnose comorbid personality disorders until the patient reached remission (Benazzi 2000).

One study (Cassas-Barquero *et al.* 2007) examined bipolar patients regardless of presence comorbid personality disorder. Results showed no significant differences regarding clinical features, but patients with comorbid personality disorder had a younger age at onset, experienced more depressive episodes and suffered by longer duration of bipolar disorder. According NICE guidelines, in subjects with comorbid personality disorders, the number of hospitalizations correlated significantly with depressive episodes (O'Dowd 2006).

CONCLUSION

Considerable amount of information is available about symptoms, time course, and management of bipolar disorder that is uncomplicated by comorbidity. However, less is known about the effects of comorbidities, particularly about comorbidity with personality disorders.

Personality traits are related to various mental disorders, particularly personality disorders. Tests of personality traits indicated that euthymic bipolar patients have higher scores on HA, RD, and NS than controls. Elevation of NS in bipolar patients is associated with substance abuse comorbidity.

Comorbidity with personality disorders in bipolar patients is accompanied by more difficult course of disorder (such as longer episodes, shorter time spending in euthymic phase, and earlier age at onset). Another problem may be increasing of comorbid substance

abuse, suicidality and aggression. These problems are particularly pronounced in comorbidity with borderline personality disorder. Comorbidity with antisocial personality disorder elicits a similar spectrum of difficulties; some of the antisocial behavior exhibited by patients with this comorbidity is mediated by increased impulsivity.

Lamotrigine or valproate alleviate symptoms of both bipolar disorder and borderline personality disorder in patients with this comorbidity. Biological relationship between bipolar disorder and borderline personality disorder is a subject of considerable ongoing research effort.

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