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Clinical and Cognitive Predictors of Psychosocial Functioning During the Euthymic Period in Bipolar Disorder Type II

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SUMMARY

Aim: Review of clinical and cognitive predictors of psychosocial functioning during the euthymic period period in patients with bipolar disorder type II (BD II) was aimed in this paper. Psychosocial functioning status, clinical and cognitive predictors of psychosocial functioning and assessment of psychosocial functioning during the euthymic period in patients with BD-II were discussed.

Method: Studies investigated psychosocial functioning and its clinical and cognitive predictors were reviewed. Studies conducted between 1990 and 2013 were scanned.

Results: It's been seen that there were limited studies investigating psychosocial functioning and predictors of psychosocial functioning. Findings from these limited studies indicated that patients with BD-II experienced psychosocial disability as much as BD-I did. It was reported that subclinical depressive symptoms and cognitive impairment were the prominent predictors of psychosocial functioning during the euthymic periods in patients with BD-II.

Conclusion: There are limited studies conducted in euthymic BD-II patients. There are various findings among the studies. Nevertheless, subclinical depressive symptoms and cognitive impairments are the prominent predictors of psychosocial functioning in euthymic BD-II patients. However, follow-up and cross-sectional studies are needed in this area.

Keywords: Bipolar DisorderType II, psychosocial functioning, cognitive function

INTRODUCTION

Bipolar disorder (BD) is a chronic disease characterized by depressive, manic, or mixed episodes, and inter-episodic illness-free periods (with or without subclinical symptoms), and causes severe social and occupational disability. Bipolar disorder type I (BD-I), bipolar disorder type II (BD-II), cyclothymic disorder, BD due to substance or drug use, other types of BD associated with other medical conditions, and BD not otherwise specified, are grouped as BD in DSM-V (American Psychiatric Association 2013)

Prevalence rates vary according to the subtype of BD. The lifetime prevalence of BD-I is 0%-2.4%, and there are no differences in the prevalence according to ethnicity, culture, or gender. The prevalence of BD-II is 0.3%-4.8% and BD-II occurs more frequently in females than in males (Rihmer and Angst 2007). The prevalence of cyclothymic disorder is 0.3%-0.6% (Lewinshon et al. 1995), the lifetime prevalence rate is 3%-6% among outpatients with cyclothymic disorder (Stewart et al. 2006), and it is more prevalent in females than males (Judd and Akiskal 2003). According to DSM-IV, the prevalence of BD is 4.5% when BD not otherwise specified is included (Merikangas et al. 2007). According to DSM-V, psychosocial impairment during episodes of illness must occur for BD to be diagnosed. As such, assessment of psychosocial functioning during inter-episodic periods (remission) is essential.

The present study aimed to review the clinical and cognitive factors that predict the level of psychosocial functioning in

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BD-II patients during euthymic periods. This literature review addresses the level of psychosocial functioning in BD-II patients during euthymic periods, the clinical and cognitive predictors of the level of psychosocial functioning in BD-II during euthymic periods, and findings related to assessment of psychosocial functioning in BD-II patients. Research conducted between 1990 and 2013 on the clinical and cognitive predictors of psychosocial functioning in BD were included. PubMed, Google Academics, and Science Direct databases were searched using the following keywords: bipolar disorder, bipolar disorder type I, bipolar disorder type II, psychosocial functioning, neurocognition, psychosocial outcome, clinical and neurocognitive predictors, meta-analysis, medication, treatment, lithium treatment, and review. Studies that included pediatric patients, and those published in languages other than Turkish and English were excluded.

A search of the afore-mentioned databases showed that the most of the relevant studies included primarily euthymic BD-I patients or patients with both BD-I and BD-II, and that there is a limited number of studies that included only euthymic BD-II patients. As such, studies that included patients with BD-I, or BD-I and BD-II are the focus of the present review, followed by studies on BD-II.

Psychosocial functioning is a complex concept, involving the capacity to work, study, live independently, and engage in recreational activities and interpersonal relationships. Functional recovery in BD has been described as the ability to achieve a level of functioning that was achieved prior to the most recent episode (Zarate et al. 2000). It was reported that allmost %50 of BD patients experience social, occupational, and interpersonal dysfunction, even while in remission (Levy and Manove 2012; Elgie et al. 2007; MacQueen et al. 2001). MacQueen et al. (2001) reviewed 17 follow-up studies that included euthymic BD patients and reported that regardless of BD subtype 30%-60% of BD patients experience occupational and social dysfunction. More recent reviews also report psychosocial impairment in BD patients (without referring to any subtypes of BD) during euthymic periods, as compared to healthy controls (Levy and Manove 2012; Sanches-Moreno et al. 2009; Wingo et al. 2009; Elgie et al. 2007; Kennedy 2007). Moreover, studies have reported that 50% of BD patients are unemployment in the long term. In addition, studies on social, cognitive, occupational, and independent functioning via self-reports indicate that 40% of BD patients have psychosocial functional impairment (Shippee et al. 2011; Huxley and Baldessarini 2007; Tohen et al. 2000;).

Follow-up studies conducted with BD patients also provide some evidence about psychosocial functioning during euthymic periods. A 2-year follow-up study reported that 97% of hospitalized BD patients with a first manic episode with psychotic features achieved syndromal recovery at the 24-month follow-up, whereas only 37% achieved functional recovery (Tohen et al. 2000). Another follow-up study noted that 90% of patients achieved syndromal recovery at the end of the 12-month follow-up, whereas 66% of patients did not achieve the same level of psychosocial functioning they had prior to the onset of illness (premorbid period) (Conus et al., 2006). Martinez-Aran et al. (2007) reported that 44% of euthymic BD patients experienced psychosocial disability. Nonetheless, a numerous cross-sectional studies reported that psychosocial impairment in BD patients persists even during euthymic periods (Tabares-Seisdedos et al. 2008; Weinstock and Miller 2008; Goetz et al. 2007; Tohen et al. 2005; Calebrese et al. 2003). These findings suggest that there is a gap between clinical and functional recovery in BD patients.

Psychosocial Functioning During Euthymic Periods in BD-II

There are limited number of studies comparing psychosocial functional outcome in euthymic BD-I and BD-II patients (Rosa et al. 2010; Sanchez-Moreno et al. 2009). For instance, Sanchez-Moreno et al. (2009) reviewed 2 studies that compared psychosocial outcome in BD-I and BD-II patients, both of which reported that no differences were observed between BD-I and BD-II patients regarding psychosocial disability during depressive and euthymic periods. Rosa et al. (2010) observed that BD-I and BD-II patients exhibited a similar pattern of functional impairment, as compared to healthy controls, except for the Functioning Assessment Short Test (FAST) (Rosa et al. 2007) cognitive domain, in which BD-II patients scored lower than BD-I patients; however, after controlling for age, subsyndromal symptoms of depression, and the number of depressive episodes, there was no longer a significant difference between the BD-1 and BD-II patients.

Similar levels of psychosocial functional impairment were also observed in patients with BD-I (n = 42) and BD-II (n = 23) (Wingo et al. 2010). Judd et al. (2005) similarly reported that there wasn't a difference in psychosocial functional outcome based on the Global Assessment of Functioning Scale between BD-I and BD-II patients. Cooke et al. (1996) reported that BD-II patients (n = 13) had lower Medical Outcomes Study Short Form (SF-20) social functioning scores than BD-I patients (n = 17). These findings support the hypothesis that BD-II causes psychosocial functional disability to the same degree as does BD-I, and that BD-II is a disorder distinct from BD-I rather than a less severe form of BD-I. No studies comparing BD-II and cyclothymic disorder or BD-II and bipolar disorder-NOS have been found in the context of psychosocial function status.

Clinical and Cognitive Predictors of Psychosocial Functioning in BD-II Patients

Clinical and cognitive predictors of psychosocial functional impairment in euthymic BD patients have been studied extensively; however, such research has focused primarily on BD-I.

Clinical Predictors of Psychosocial Functioning in Euthymic BD-II Patients

Recent reviews report that subclinical symptoms of depression, comorbidity, the number of prior hospital admissions, the number of prior episodes, and history of psychotic and manic episodes negatively affect psychosocial functioning in euthymic BD-I patients (Levy and Manove 2012; Treuer and Tohen 2010; Mac Queen et al. 2001). Sanchez-Moreno's (2009) review reported that subclinical symptoms of depression, persistent neurocognitive impairment, and comorbid substance use and comorbid anxiety disorders are the most important predictors of psychosocial impairment in euthymic BD patients.

Cross-sectional studies have reported that some clinical factors are associated with poor functional outcome in BD, including comorbid substance use (Tohen 1998), the side-effects of medication (Zarate et al. 2000), history of psychotic symptoms (Tohen et al. 2000; Tohen et al. 1990), low level of premorbid functioning (Cannon et al. 1997), persistent subsyndromal symptoms (Martinez-Aran et al. 2004; Gitlin 1995), the number of prior episodes (MacQueen et al. 2000; Tohen et al. 1990), and younger age of onset (Rosa et al. 2009; Tohen et al. 2000).

The literature indicates that subclinical symptoms of depression and comorbidity commonly cause poor psychosocial functional outcome in euthymic BD-I patients; however, it's also been stated that there is a difficulty to replicate these findings. (Rosa et al. 2009; Wingo et al. 2009; Sanchez-Moreno et al. 2009; Martinez-Aran et al. 2007). Inconsistent findings and difficulty in replicating results have been associated with the fact that most of the relevant studies included patients with current mood symptoms, did not use modern diagnostic symptomatic remission criteria for euthymic periods or diagnostic criteria, relied on non-objective self-report instruments, assessed global functioning, failed to take into account the specific domains of psychosocial functioning for an optimal functioning, and used different instruments to assess psychosocial functioning (Andreu and Bozikas 2013; Bonnin et al. 2010; Rosa et al. 2010, 2009; Sanchez-Moreno et al. 2009; Wingo et al. 2009; Martinez-Aran et al. 2007; MacQueen et al. 2001). As such, it remains unknown if the factors reported to negatively affect psychosocial functioning in BD, such as the number of previous episodes, younger age of onset, psychiatric comorbidity, neurocognitive impairment, and subclinical symptoms of depression, can be applicable to BD-II, but some cross-sectional studies indicate that they can.

Rosa et al. (2010) reported that subclinical symptoms of depression and middle-old age predicted psychosocial functional impairment in euthymic BD-II patients (n = 61). Wingo et al. (2010) observed that euthymic BD-I patients (n = 42) and euthymic BD-II patients (n = 23) experienced a similar level of psychosocial functional impairment, which was associated with younger age of onset and subclinical symptoms of depression. Another cross-sectional study (Rosa et al. 2009) in which euthymic BD-I patients (n = 48), euthymic BD-II patients (n = 23), and healthy controls (n = 61) were compared reported that the number of previous mixed episodes, current subclinical symptoms of depression, the number of previous hospital admissions, and older age were associated with psychosocial functional impairment in euthymic BD patients. Torrent et al. (2006) also reported that subclinical symptoms of depression negatively affect psychosocial outcome and cognitive functioning. Moreover, it was reported that BD-II patients experience longer depressive periods, have more depressive episodes, and have shorter euthymic periods than BD-I patients (Vieta et al. 1997; Judd et al. 2003), and that depressive episodes in BD-II patients are more severe than those in BD-I patients (Benazzi 2001). It was also was reported that the number of depressive episodes negatively affects psychosocial outcome (MacQueen et al. 2001). These findings indicate that as the number of depressive episodes increases and the duration of interepisodic periods decreases in BD-II patients the risk of residual symptoms of depression increases (Benazzi 2001).

Cognitive Predictors of Psychosocial Functioning in Euthymic BD-II Patients

Recent meta-analyses reported that BDI-I patients have neurocognitive impairment during euthymic periods that range from intermediate to moderate, especially in the domains of executive functions, verbal learning, and memory, as compared to healthy controls (Bourne et al. 2013; Bora et al. 2009; Kurtz and Gerraty 2009; Arts et al. 2008; Torres et al. 2007; Robinson et al. 2006). These findings suggest that psychosocial functioning might be associated with cognitive functions; as such, the number of studies on the contribution of cognitive deficits to psychosocial outcome in BD patients has been increasing. Our search showed that there are 5 relevant published reviews (Andreu and Bozikas 2013; Levy and Manove 2012; Wingo et al. 2009; Sanchez-Moreno et al. 2009; Kennedy et al. 2007). Andreu and Bozikas (2013) reviewed 12 studies that included primarily BD-I patients and reported that cognitive deficits in euthymic patients predicted the level of psychosocial functional outcome. Levy and Manove (2012) reviewed 11 follow-up studies in which most of the patients had BD-I and reported that cognitive deficits, particularly in the domain of executive functions, had a negative effect on the level of psychosocial functioning. Wingo et al. (2009) examined 8 studies that primarily included BD-I patients and reported that there was a linear association observed between cognitive deficits and psychosocial functional impairment in the 6 of the 8 studies. In particular, verbal learning and memory, executive functions, attention, and

processing speed predicted psychosocial functional impairment (Wingo et al. 2009). Sanchez-Moreno et al. reviewed 4 studies and reported that verbal memory deficit was associated with psychosocial functional disability. Another review conducted by Kennedy et al. (2007) reported that cognitive deficits during euthymic periods had a negative effect on psychosocial functional outcome.

Reviews have consistently reported that cognitive impairment during euthymic periods causes psychosocial functional impairment; however, an association between cognitive deficits and psychosocial functional impairment was not observed by Kaya et al.'s (2009) study on euthymic BD-I patients (n = 43). Malhi et al. (2007) reported that psychosocial functional impairment could not been explained by only by cognitive deficits. These 2 study's findings were associated with subclinical affective symptoms and psychosocial functional impairment. Recent reviews, follow-up studies, and cross-sectional studies report inconsistent findings, indicating that more longitudinal studies with larger samples are needed, as only a limited number of studies have investigated the factors associated with psychosocial functioning and most such studies used self-reports and different instruments to assess functioning (Martinez-Aran et al. 2007; Dean et al. 2004; Pachet and Winsniewski 2003).

A meta-analysis reported that euthymic BD-I and euthymic BD-II patients had similar cognitive deficits, in general (Bora et al. 2011). The researchers investigated 12 studies that compared cognitive functioning in euthymic BD-I and BD-II patients, and reported that cognitive deficits were similar in the BD-I and BD-II patients, whereas verbal memory, visual memory, and semantic deficits were more common in BD-I patients. The findings of recent cross-sectional studies (Sole et al. 2012; Martino et al. 2011) are similar to those reported by Bora et al. (2011). The studies have shown that euthymic BD-II patients may have cognitive impairment in the domains of executive functions, working memory, and attention that are similar in severity and quality as those observed in BD-I patients, which indicates that the association between cognitive dysfunction and psychosocial functioning is similar in BD-I and BD-II.

To the best of our knowledge only 2 studies have investigated the association between cognitive functions and psychosocial functioning in euthymic BD-II patients (Sole et al. 2012; Torrent et al. 2006). Torrent et al.'s (2006) cross-sectional study reported that there is an association between Trail Making Test (TMT-B) scores (TMT-B is used to assess executive functions) and psychosocial functional impairment in euthymic BD-II patients (n = 33). Similarly, Sole et al. (2012) noted an association between executive functions (TMT-B score) and psychosocial functional impairment in their cross-sectional study that included 43 euthymic BD-II patients and 43 healthy controls. These findings suggest that deficits in the cognitive domains of executive functions and working memory (Torrent et al. 2006) might be predictors of psychosocial functional impairment in euthymic BD-II patients; however, the validity of these findings are questionable due to the limited number of studies that investigated the association between cognitive deficits and psychosocial functioning, ambiguity of comorbidity, the limitations of the flexible remission criteria, small samples, any follow-up studies, the limited studies that compared euthymic BD-I and BD-II patients and the elusiveness of the association between cognitive functions and drug effect.

Assessment of Psychosocial Functioning in BD

Assessment tools have recently become a focus of interest following the successful control of the clinical symptoms of BD (Aydemir and Uykur 2012). To date, studies that have assessed psychosocial functioning in BD have used different assessment instruments. Dean et al. (2004) investigated 13 scales that are utilized to assess psychosocial functioning in BD. They reported such scales as the Short Form-36 (SF-36), Levenstein-Klein-Pollack Scale, Specific Level of Functioning Scale, Streamlined Longitudinal Interview Clinical Evaluation, and Longitudinal Interval Follow-up Evaluation were not specific to BD, but are also used to assess psychosocial functioning in other disorders. The World Health Organization Disability Assessment Scale (WHO-DAS), Global Assessment of Functioning (GAF), Social and Occupational Functioning Assessment Scale (SOFAS), Social Adjustment Scale (SAS), and Life Functioning Questionnaire (LFQ) were also reported to be other instruments used to assess psychosocial functioning in BD patients (Rosa et al. 2007). Assessment instruments, such as FAST (Aydemir and Uykur 2012), SF-36 (Kocyigit et al. 1999), WHO-QOL (Fidaner et al. 1999), Social Functioning Scale (Erakay 2001), Individual and Social Performance Scale (Aydemir et al. 2009), WHO-DAS (Ulug et al. 2001), and Q-LES-Q (Ozer et al. 2001) have Turkish forms that were reported to be valid and reliable for use in Turkey. GAF and SOFAS which are included in DSM IV were also translated to Turkish (American Psychiatric Association 1994)

The findings of studies on psychosocial functioning in BD are inconsistent and difficult to replicate due to the use primarily of self-report assessment instruments and lack of assessment based on clinician observations (Dean et al. 2004). Assessment tools designed to measure psychosocial functioning in euthymic BD patients are extremely long, difficult to administer in clinical settings, and measure global or limited functioning status rather than specific, discrete domains of psychosocial functioning (Strakowski et al. 2000; Zarate et al. 2000). Moreover, instruments developed to assess specific domains of functioning in BD are insufficient because they

fail to take into account the cognitive and financial measures (Rosa et al. 2007).

FAST was developed by Rosa et al. (2007) to assess the various domains of psychosocial functioning, and the Turkish version was reported to be reliable and valid for use in Turkey (Aydemir and Uykur 2012). This scale is suggested by researchers to utilize in researches due to the fact that it allows assessing of specific domains of psychosocial functioning. In addition, the Bipolar Disorder Functioning Questionnaire (BFQ) developed by Aydemir and Uykur (2007) is also used to assess psychosocial functioning. Based on published data, it can be said that using the scales (FAST and BFQ) to assess psychosocial functioning will provide more comprehensible evidence and reliable findings in this topic.

To our knowledge, any studies conducted with other subtypes of bipolar disorder have been found in the context of psychosocial functioning.

DISCUSSION

Despite the fact that there are a limited number of studies on euthymic BD-II patients, the findings indicate that euthymic BD-II patients have a level of psychosocial functional disability similar to that in euthymic BD-I patients. Both BD-I and BD-II patients have been included in studies that assessed psychosocial functioning, and the findings support the hypothesis that psychosocial functioning in BD-II patients is impaired during euthymic episodes. Evidence to date shows that subclinical symptoms of depression and cognitive impairment are the key predictors of psychosocial functional impairment in euthymic BD patients (Sanchez-Moreno et al. 2009). In addition, the number of prior episodes, younger age of onset, middle-old age, the number of manic and psychotic episodes, the number of prior hospital admissions, the number of suicide attempts, presence of comorbid substance use and anxiety disorders, and the number of depressive episodes are other factors associated with psychosocial functional impairment; however, there are insufficient studies whereas these results are applicable to BD-II or not. According to the limited number of available studies, it is clear that subclinical symptoms of depression and cognitive impairment are the most important predictors of psychosocial functional impairment in euthymic BD-II patients. To the best of our knowledge the present study is the first to review the literature on the association between clinical factors, and cognitive functioning and psychosocial functioning in euthymic BD-II patients.

According to earlier reviews, there isn't a consensus concerning if cognitive deficits occur during premorbid periods in BD-II patients or if cognitive deficits exacerbate during the course of illness. In addition, it's clear that more follow-up studies and family-based studies are needed in order to discern the progression of cognitive functions and its impact on psychosocial functioning in euthymic BD-II patients.

Patients with BD-II experience deficits in the domains of executive functions, working memory, and attention, especially during euthymic periods (Bora et al. 2011). Some researchers suggest that verbal learning and memory deficits, which are found in some studies, are derived from the differences between the assessing methods to measure the verbal learning and memory (Sole et al. 2011). Nonetheless, research indicates that euthymic BD-II patients experience the same level of cognitive deficits in the domains of executive functions and working memory as do euthymic BD-I patients (Bora et al. 2011; Sole et al. 2011).

Some studies have investigated the association between cognitive deficits and psychosocial functioning in euthymic BD-II patients (Sole et al. 2012; Torrent et al. 2006). Nevertheless, due to the similarity in cognitive deficits in euthymic BD-I and BD-II patients, it can be considered that cognitive deficits in euthymic BD-II patients might be predictive of psychosocial functional impairment. The findings reported by the cross-sectional studies performed by Sole et al. (2012) and Torrent et al. (2006) support this hypothesis; however, the findings should be considered with caution due to the studies' limitations, such as small sample size, use of global measures (GAF and SOFAS), and inclusion of poly-medicated patients.

The literature shows that the potential effect of comorbidity on psychosocial functioning has not been investigated in euthymic BD-II patients. Thus, substance use disorder, anxiety disorders, and attention deficit-hyperactivity disorder should be included in the differential diagnosis of comorbid states. To date, the effects of medication on psychosocial functioning have not been comprehensively investigated, which is another limitation of the literature. As it is well known that medications can negatively affect psychosocial functioning directly, it might cause unremitted clinical symptoms (such as residual and subclinical affective symptoms), extrapyramidal symptoms, or psychosocial functional impairment via negative effects on cognitive functioning (Senturk et al. 2007).

In general, global assessment tools (such as SOFAS and GAF) have been used to assess psychosocial functioning. Instruments that assess discrete and specific domains of psychosocial functioning, such as occupation, cognition, social relationships, finances, interpersonal relationships, and autonomy, have been used in only a limited number of studies (Rosa et al. 2010). As such, it is difficult to precisely measure the level of psychosocial functioning in patients, and its clinical and cognitive predictors. Assessing the specific and discrete domains of psychosocial functioning in euthymic BD-II patients is essential, because euthymic BD-II patients can have the same level of psychosocial impairment as euthymic

BD-I patients. As such, it's been suggested that practical, new assessment instruments similar to FAST should be developed for assessing the specific domains of psychosocial functioning (Sole et al. 2012).

Lastly, the literature also indicates the importance of investigating subclinical symptoms of depression and cognitive deficits in BD, which are the best-known predictors of psychosocial functional impairment, as such research is likely to contribute to the design of treatment and follow-up plans for BD-II patients undergoing psychosocial rehabilitation.

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