

Cognitive and psychosocial impairment in remitted bipolar patients

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Artículo

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Abstract

Bipolar disorders constitute a complex group of recurrent mental illnesses with high prevalence among general population. The current systems of classification, such as CIE–10 and DSM–5, represent a significant advance for their accurate identification. However, there is still a relevant delay on their diagnoses. The present paper describes the more distinctive clinical features of these illnesses, discuss the general concepts regarding of bipolar spectrum, mixed states, clinical differences between unipolar and bipolar depression, and the differential clinical criteria with other disorders.

Keywords: Euthymic bipolar disorder – Cognition – Psychosocial functioning.

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Bipolar disorder is a chronic mental disorder, found in approximately 4% of the population, and characterized by extreme changes in mood polarity (mania and depression) with intervening periods of euthymia (Merikangas et al., 2007). However, these periods of clinical remission (euthymia) are marked by subtle social, occupational, and cognitive dysfunctions. Although cognitive impairments are associated with acute mood episodes, they seem to persist, in lower degree, even during periods of euthymia (Torres, Boudreau, & Yatham, 2007). The exact meaning and impact of cognitive deficits in bipolar disorder is still not entirely known, even though they have been associated with poorer psychosocial functioning (Sanchez–Moreno et al., 2009; Wingo, Harvey, & Baldessarini, 2009). Impairment in cognitive functioning and inability to perform adequately everyday life situations are prevalent, in various degrees, in bipolar disorder, despite modern therapeutic advances (Huxley & Baldessarini, 2007). Many patients with bipolar disorder do not regain their premorbid level of occupational functioning even after recovering from mood episodes. This disorder is also characterized by marked heterogeneity in symptomatology, treatment response, clinical course and outcome.

The aim of the present review is to summarize results from studies assessing cognitive and psychosocial functioning of remitted bipolar patients.

Methods

The authors conducted an extensive Medline search of the published English literature for the period from January 2000 to March 2014. We selected documents containing, in the title and abstract sections, the descriptors *cognition*, *cognitive impairment*, *neuropsychological test*, *psychosocial functioning*, *functional impairment*, *social functioning* and *bipolar disorder*. Abstracts and titles were used to determine whether the reference might be relevant to the review, and full texts of potentially relevant articles were retrieved to assess the article for inclusion. The articles were selected if they met the following quality criteria: bipolar disorder patients on euthymia state, cross–sectional or longitudinal studies, clinical trials, systematic reviews and meta–analyses, including standardized diagnostic criteria (Diagnostic and Statistic Manual of Mental Disorders) and well–defined cognitive and functioning measures. Finally, the reference lists of retrieved articles were checked for any further relevant citations. We focused on three specific points: (1) What are the most affected cognitive domains in euthymic bipolar patients; (2) Is there any association between cognition and clinical course of the illness; (3) What is the role of cognitive functioning on psychosocial functioning in remitted bipolar patients.

Results

The main cognitive deficits found in euthymic bipolar patients

In the last decade, a growing interest has emerged regarding the cognitive functioning in mood disorders. A number of reports have documented an association between bipolar disorder and persistent cognitive deficits. It has been suggested that cognitive impairment is a core feature of bipolar disorder (Goodwin, Martinez–Aran, Glahn, & Vieta, 2008; Martinez–Aran et al., 2004a), which occurs across cultures (Goswami et al., 2006; Robinson et al., 2006). Patients with bipolar disorder generally exhibit typical cognitive development pre–morbidly (Quraishi & Frangou, 2002; Torres et al., 2007), but demonstrate deficits by first episode that are amplified with worsening symptoms and exacerbations. Prospective studies are few, but there is evidence of stable and lasting cognitive impairment during acute and euthymic phases of the illness (Balanza–Martinez et al., 2009; Mann–Wrobel, Carreno, & Dickinson, 2011; Mur, Portella, Martinez–Aran, Pifarre, & Vieta, 2008). Many individuals with bipolar disorder respond well to treatments designed to reduce affective and psychotic symptoms, therefore these individuals persist showing cognitive impairment even after prolonged asymptomatic phases (Zubieta, Huguelet, O’Neil, & Giordani, 2001). All mood states of bipolar disorder are associated with cognitive impairment. However, the euthymic state is associated with less impairment than the other states (Malhi et al., 2007; Martinez–Aran et al., 2004b). Furthermore, the cognitive dysfunctions of bipolar and schizophrenic patients are similar. However, the severity of such dysfunctions are greater in schizophrenia (Sanchez–Morla et al., 2009).

A number of comprehensive reviews and meta–analyses of neuropsychological performance indicated that euthymic patients with bipolar disorder show impairments on tests of attention, processing speed, verbal memory and several aspects of executive function. Indeed, four meta–analysis indicated large effect sizes for executive functioning in euthymic bipolar patients relative to healthy controls (Arts, Jabben, Krabbendam, & van Os, 2008; Bora, Yucel, & Pantelis, 2009; Robinson & Ferrier, 2006; Torres et al., 2007). Other two meta–analyses, however, have concluded that cognitive impairment in euthymic bipolar disorder is generalized rather than specific (Kurtz & Gerraty, 2009; Mann–Wrobel et al., 2011). In this regard, it has been suggested that executive functioning is a multifaceted construct that can refer to a broad range of processes including planning, motivation, and inhibition. Robinson et al. (2006) report their large effect sizes in this domain as not being reflective of

a wide executive dysfunctions syndrome, but as evidence of more selective deficits. While medium-to-large effect sizes have been detected for measures of certain aspects of executive function (especially response-inhibition and set-shifting tasks) not all executive functions are equally impaired in bipolar patients (Yatham et al., 2010). Verbal learning and memory deficits, for example, are frequently reported among euthymic bipolar patients. Robinson and Ferrier (2006) have also discussed about the potential overlap between executive functioning and verbal learning suggesting that executive deficits may affect memory performance and also suggesting that more research are needed to establish whether one or two domains of functioning are reliably impaired in bipolar disorder.

The most recent meta-analyses (Bourne et al., 2013) showed that euthymic bipolar patients exhibit substantial cognitive impairment on neuropsychological tests, especially on attention/working memory, verbal memory, speed and executive function. Such deficits remain significant even after controlling for confounders factors such as age, IQ and gender. However, the effect sizes for cognitive deficits were lower than those reported in prior meta-analyses. This reduction in effect sizes is in part due to controlling better for the confounders and variations on the studies included.

Finally, some discrepancies between neurocognitive studies in psychiatry have been documented in the literature. This happens partly because of the lack of homogeneity regarding the neuropsychological measures used in such reports. In general, the assessment of neuropsychological performance is carried out by specific tests that allow us to assess qualitative and quantitative analysis of patients' cognitive performance (Lezak, 1995). Nevertheless, no consensus about the most appropriate cognitive battery for bipolar disorder research was reached until few years ago. So, in 2010, International Society for Bipolar Disorders (ISBD) established a committee of experts that proposed a preliminary battery that could be applicable for international use in bipolar disorder. This committee suggested that the main domains to assess cognition in bipolar patients are: speed of processing, attention/vigilance, working memory, verbal learning/memory, visual learning and executive function. It represents a good starting point for the assessment of cognition in bipolar disorder as offers a standardization of the instruments used in setting research. The wider adoption of a common set of standardizes procedures will lead to results that will be more comparable across different research groups spanning the international community, and this is likely to facilitate research and accelerate the acquisition of knowledge pertaining to cognitive impairment in bipolar disorder (Yatham et al., 2010).

The relationship between course of the illness and cognitive functioning

There is increasing evidence showing that cognitive functioning may be influenced by the course of the bipolar illness (Martinez–Arán et al, 2004a, 2004b, 2007; Sanchez–Moreno et al., 2009; Zubieta et al, 2001). Particularly, the impact of number of manic episodes has been pointed out as a good predictor of cognitive performance in bipolar disorder. Patients with more than two episodes of mania are more impaired in executive function, memory and psychomotor speed domains than those with only one manic episode (Lopez–Jaramillo et al., 2010). Psychotic symptoms are another variable that has been associated with poor cognition as patients with a history of psychosis experienced greater impairment on verbal memory and executive function than those without symptoms (Levy & Weiss, 2010).

The impact of the course of the illness on cognitive functioning has been also corroborated by distinct longitudinal studies. For instance, a 6–year–follow–up study conducted in euthymic bipolar patients demonstrated marked deficits on executive function, inhibition, processing speed and verbal memory; such deficits persisted over time and were more pronounced in patients with advanced stage of the illness (e.g., longer illness duration) than those in the early stages (Mora, Portella, Forcada, Vieta, & Mur, 2013). Similarly, another study demonstrated that cognitive impairment tends to remain stable across the 9–year–follow–up period in many cognitive measures, except for a worsening in executive function and a slightly improvement in attention (Torrent et al., 2012). In addition, this study showed that duration of illness and subclinical depressive symptoms were associated with worse performance in executive function. The presence of subclinical depressive symptoms has been related to deficits on memory as well (Bonnín et al., 2012). Furthermore, verbal learning and memory dysfunctions and residual depressive symptoms were the best predictors of 4–year outcome (Bonnín et al., 2010). Recently, a meta–analysis conducted by Bourne et al. (2013) suggests that residual depressive symptoms as well as side effects of medications may also contribute to cognitive impairment in euthymic bipolar sample. However, the effect of pharmacologic treatment on cognition is still uncertain due to a lack of randomized comparative trails in this issue (Vieta, 2009).

Many of these clinical measures (duration of illness, number of episodes and number of hospitalizations) are highly intercorrelated, and could be considered as a single “longitudinal severity of illness factor” (Robinson & Ferrier, 2006). Therefore, although cognitive impairment is likely influenced by clinical course of the illness, these factors do not appear to account fully for the neuropsychological impairments observed in remitted patients. Though evidence suggests that greater neuropsychological dysfunction in bipolar disorder is associated with a worse

prior course of illness, the direction of causality as cognitive impairment is unclear. It may be the cause or consequence of poor clinical course.

The role of cognitive impairment on psychosocial functioning in euthymic bipolar patients

Functional impairment has been related to many severe mental illnesses, including bipolar disorder. According to National Comorbidity Survey replication study, patients with bipolar disorder in remission reported higher impairment on social and interpersonal relationships than subjects with chronic medical disorders, including cancer, heart disease, diabetes mellitus, rheumatoid arthritis, and renal failure (Robb, Cooke, Devins, Young, & Joffe, 1997). Bipolar patients experience poor functioning in multiple areas such as independent living, interpersonal relationships, occupational and educational achievement, recreational enjoyment, and sexual activity (Rosa et al., 2010a). In fact, according to World Health Organization (2008), bipolar disorder is the sixth leading cause of years lost due to disability in young adults (Murray & Lopez, 1997).

Psychosocial dysfunctions are not limited to symptomatic periods, but seem to continue for prolonged periods, despite the remission of symptoms (Rosa et al., 2011). For instance, Huxley and Baldessarini (2007) reported that despite of modern treatments, 90% of patients achieved syndromal recovery, whereas only 1/3 of total sample achieving functional recovery (defined by their own premorbid levels). This persistent psychosocial impairment may contribute to high personal suffering and socioeconomic costs to society.

Mood symptoms have been significantly associated with functional impairment in bipolar disorder (Rosa et al., 2010b; Simon, Bauer, Ludman, Operskalski, & Unutzer, 2007). In general, symptoms of depression have been associated with functional role impairment in multiple domains such as duties at work or school, responsibilities at home, and relationships with family and friends (Simon et al., 2007). Other clinical variables such as previous mixed episodes, subclinical depressive symptoms, number of hospitalizations and older age appear to have a negative impact on functioning (Rosa et al., 2009)

Furthermore, cognitive impairment may play a significant role on functioning of bipolar disorder patients (see figure 1). For instance, Martinez–Aran et al. (2007) reported that psychosocial functioning in bipolar patients was associated with neuropsychological measures rather than with clinical variables. In particular, poor frontal executive functioning and verbal and learning memory were significantly associated with psychosocial impairment. Deficits in memory, attention, and planning may lead to impairment in social, interpersonal, and

occupational functioning, and these deficits make it difficult to undertake occupational tasks or engage in interpersonal relationships (Martinez–Aran et al., 2007). It has been demonstrated that cognitive deficits were associated with lower long–term functioning in distinct follow–up studies (Bonnín et al., 2010; Martino et al., 2009; Mora et al., 2013; Torrent et al., 2012). A 4–year follow–up study conducted by Bonnín et al. (2010), in a euthymic bipolar sample, showed that verbal memory was the best predictor of long–term functional outcome. Similarly, attention and verbal fluency were identified as predictors of outcome at 12 months in a sample of 35 patients with bipolar disorder type I (Martino et al., 2009). Subclinical depressive symptoms and verbal memory emerged as significant predictors of poor functioning in a 9 years follow–up (Torrent et al., 2012).

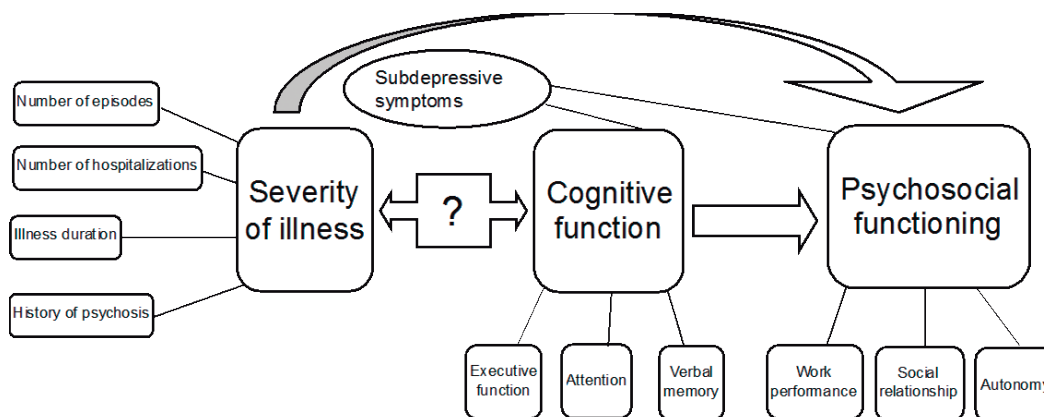


Figure 1. The main factors associated with cognitive and psychosocial impairment in bipolar disorder

Interestingly, our previous studies showed that patients with first episode had better overall functioning than those with multiple episodes, suggesting the importance of the course of the illness on long–term outcome (Rosa et al., 2012). Likewise to previous studies, recently we found that cognitive and psychosocial functioning vary according to the stage of the illness, as patients at early stages of bipolar disorder may have preserved functioning than those with late stages (Rosa et al., 2014).

Taken together, these findings support that cognitive performance may play a role on psychosocial functioning in bipolar disorder. On the other hand, it highlights the importance of development of new therapeutic strategies focused on cognitive rehabilitation as well as functional remediation in order to improve long–term outcome in bipolar patients.

Conclusions

In conclusion, this review reported that bipolar disorder patients experience cognitive deficits across mood states (mania, depression and euthymia); such deficits tend to be progressive over the course of illness and correlated with functional decline. In particular, impairment in executive functions and memory has been tied to difficulties in accomplishing tasks of daily living as well as diminished quality of life. Thus, although cognitive impairment in bipolar disorder is not completely incapacitating, the balance of the data suggests that it generates significant disruption to social and occupational adjustment. Nevertheless, the development of treatments focused on cognitive improvement and functional status is an important area of future investigation in bipolar disorder.

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