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Research report

Neurocognitive and symptomatic predictors of functional outcome in bipolar disorders: A prospective 1 year follow-up study

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ABSTRACT

Background: The aim of this study was to estimate the predictive value of cognitive impairments and time spent ill in long-term functional outcome of patients with bipolar disorder (BD).
Methods: Thirty five patients with euthymic BD completed a neurocognitive battery to assess verbal memory, attention, and executive functions at study entry. The course of illness was documented prospectively for a period longer than 12 months using a modified life charting technique based on the NIMH life-charting method. Psychosocial functioning was assessed with the General Assessment of Functioning (GAF) and the Functioning Assessment Short Test (FAST)at the end of follow-up period when patients were euthymic.
Results: Impairments in verbal memory and in attention, as well as subsyndromal depressive symptomatology were independent predictors of GAF score at the end of the study explaining 43% of variance. Similarly, impairments in attention and executive functioning were independent predictors of FAST score explaining 28% of variance.
Limitations: We did not control factors that could affect functional outcome such as psychosocial interventions, familiar support and housing and financial resources.
Conclusions: Both cognitive impairments and time spent with subsyndromal depressive symptomatology may be illness features associated with poorer long-term functional outcome. Developing strategies to treat these illness features might contribute to enhance long-term functional outcome among patients with BD.

1. Introduction

Bipolar disorder (BD) has been identified by the World Health Organization as the sixth cause of disability among all medical illness (Murray and Lopez, 1996). Different studies found that patients with BD have reduced ability to regain premorbid levels of social and vocational functioning even after episodes remission suggesting that it exists a gap between syndromal recovery and functional recovery (Keck et al., 1998; Tohen et al., 2003; Strakowski et al., 1998). Research into this area is a critical issue to clarify which illness features produce disability and targeting treatments to enhance functional outcome.

An illness feature related with the gap between syndromal and functional recovery might be cognitive impairments. Two meta-analyses concluded that euthymic patients with BD have impairments in verbal memory, attention, and executive functions (Robinson et al., 2006; Torres et al., 2007). Likewise, several studies showed a negative association between cognitive functioning and different measures of disability. Martinez-Arán et al. (2004) reported that impairments in verbal memory are associated with lower scores in measures of psychosocial functioning. Similarly, Zubieta et al. (2001) found a negative correlation between impairments in verbal memory and executive functions with social and occupational functioning, and Dickerson et al. (2004) reported a significant

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association between impairments in verbal memory with employment status. In addition with these cross-sectional findings, there is a paucity of information about if cognitive impairments would predict long-term functional outcome. A notable exception was a recent study by Jaeger et al. (2007) in which BD patients hospitalized for acute exacerbation underwent a neurocognitive battery after 'initial stabilization', and impairments in attention and ideational fluency (a measure of executive functions) were associated with functional recovery assessed 12 months later.

However, some methodological issues must be considered in studies assessing the predictive value of cognitive impairments in long term functional outcome. First, cognitive impairments have been associated with both syndromal (Martinez-Arán et al., 2004) and subsyndromal (Ferrier and Thompson, 2002; Clark et al., 2002) symptomatology, as well as with number of episodes (for a review see Robinson and Ferrier, 2006). On the other hand, long-term follow up studies showed high levels of sustained symptomatic morbidity (around 50% of time) in patients with bipolar I and II disorder, with a symptomatic structure fluctuating along the full range of severity and polarity within the same patient over time (Judd et al., 2002; Judd et al., 2003). Finally, it has been reported that disability in BD fluctuates in parallel with changes in affective symptoms severity, with exception of subsyndromal hypomanic symptoms that appear to enhance functioning (Judd et al., 2005). These inter-relationships between cognitive impairments, symptomatic status, and disability conduct to the question about potential confounders in studies assessing the predictive value of cognitive impairments in long term functional outcome. In other words, the association between cognitive impairments and long term functional outcome would be artificial and mediated by a higher number of episodes or more time spent ill during the follow up in those patients with poorer cognitive functioning. A methodological design that would be useful to avoid these potential confounders may consist in assess cognitive functioning and disability in euthymic BD patients as well as the time that they spend ill along the follow up period.

The aim of this study was to estimate the predictive value of cognitive impairments in long-term functional outcome in patients with BD. Taken into account the results of previous studies mentioned above, we hypothesize that cognitive impairments would be independent predictors of long-term functional outcome.

2. Methods

Thirty five outpatients with BD were consecutively selected with the following inclusion criteria: 1) age between 18 and 55 years old; 2) diagnosis of BD type I or II according to DSM-IV using Structured Clinical Interview for DSM-IV (SCID) (First et al., 1996); 3) euthymic (defined by Hamilton Depression Rating Scale $\leq$8 and Young Mania Rating Scale $\leq$6) for at least 8 weeks at baseline; and 4) more than 48 weeks of prospective follow up. Exclusion criteria were: antecedent history of substance abuse; history of mental retardation, neurological disease, or any clinical condition that could affect cognitive performance. Additionally, thirty healthy controls matched by age and years of education were included: these had not antecedence of neurological disease, neither history of psychotic or affective disorders in themselves or a first-degree family member, and they were not taking psychotropic medication. The study was approved by the Hospital Ethics Committee and all subjects gave written informed consent for their participation after receiving a complete description of the study.

2.1. Neurocognitive assessment

Patients and healthy controls completed a neurocognitive battery selected to assess: 1) Attention. Forward Digit SPAN (Wechsler, 1955); and Trail Making Test part A (Reitan, 1958); 2) Verbal memory: Memory Battery of Signoret (Signoret and Whiteley, 1979). This test evaluates immediate and delay recall of a short story, and the serial learning of a twelve word list of different semantic categories (3 trials), free delay recall, and recognition with semantic clues and multiple options of them; and 3) Executive functions: Wisconsin Card Sorting

	January	February	
+4			Severe Mania (YMRS>26)
+3			Moderate Mania (YMRS>16 and <25)
+2			Mild Mania (YMRS>9 and <15)
+1			Subsyndromal Mania (YMRS>4 and <8)
0			Euthymic (YMRS<4 and HDRS<4)
-1			Subsyndromal Depression (HDRS>5 and <9)
-2			Mild Depression (HDRS>10 and <15)
-3			Moderate Depression (HDRS>16 and <25)
-4			Severe Depression (HDRS>26)

Fig. 1. Criteria for assigning mood state scores in life charts.