Research Report

The impact of cognitive impairment, neurological soft signs and subdepressive symptoms on functional outcome in bipolar disorder

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ABSTRACT

Background: Cognitive impairments and subsyndromal depressive symptoms are present during euthymic periods of bipolar disorder (BD). Most studies have determined that cognitive impairments and residual depressive symptoms have major impacts on psychosocial functioning. The aim of the present study was to identify the major factor responsible for low psychosocial functioning in a subgroup of patients with BD despite clinical recovery.

Methods: Sixty patients with bipolar I disorder and 41 healthy subjects were enrolled in this study. Cognitive performance, neurological soft signs (NSSs), psychosocial functioning, residual mood symptoms and illness characteristics were assessed. Using the median value of the Functioning Assessment Short Test (FAST) as the cut-off point, the patients were divided into two groups, high- ($n=29$) or low-functioning ($n=31$), and they were compared based on total NSS, residual depressive symptoms, cognitive performance and clinical variables.

Results: Performances on the verbal memory tests and social functioning were significantly worse in the euthymic patients with BD. Increased rates of NSS were identified in the patients compared with the normal controls. The low-functioning patients performed significantly worse on verbal memory, and their NSS and residual depressive symptoms were significantly higher compared to high-functioning patients. In the regression analysis, subsyndromal depressive symptoms and verbal learning measures were identified as the best predictors of psychosocial functioning.

Limitations: The patients were artificially separated into two groups based on a FAST score cut-off.

Conclusions: In this study, residual depressive symptoms and verbal memory impairments were the most prominent factors associated with the level of functioning.

1. Introduction

Functional disability in bipolar disorder (BD), despite optimal treatment with mood stabilizers and second-generation antipsychotics, is a serious problem. Even with syndromal remission, a subgroup of patients with BD has significant difficulties with daily life activities, such as working regularly, sustaining social relationships, and engaging in family life (Bonnín et al., 2014a; Haro et al., 2011; Rosa et al., 2009). Previous research has suggested that the gap between symptomatic remission and concepts such as quality of life, employment and capacity to live independently is substantially independent of clinical variables, such as the number of episodes, the number of hospitalizations and the duration of illness (Martinez-Aran et al., 2007). Social dysfunction is manifested even at the very beginning of the illness in a subgroup of patients (Tohen et al., 2000).

Many studies have identified depressive symptoms as the major factor that is responsible for poor psychosocial outcomes in patients with BD (Bonnín et al., 2010; Gitlin et al., 1995; Judd et al., 2005; Strejilevich et al., 2013). Depressive symptoms even at the subsyndromal level have been found to produce cognitive effects, predominantly on verbal memory (Bonnín et al., 2012; Torrent et al., 2012). Poor cognition, particularly verbal memory deficits, has been linked to poor psychosocial functioning in many studies (Bonnín et al., 2010; Martino et al., 2009). There is a complex interaction among neurocognition, psychosocial outcome and residual depressive symptoms. A recent prospective study

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demonstrated that verbal memory mediated the relationship between depression and poor cognition (Bonnín et al., 2014b).

Neurological soft signs (NSSs) have been observed in patients with bipolar disorder (Goswami et al., 1998, 2006; Nasrallah et al., 1983). Furthermore, NSSs are regarded as markers of frontal lobe dysfunction in bipolar disorder. In a previous study, NSSs were strongly correlated with social dysfunction in patients with bipolar disorder (Goswami et al., 2006).

We compared cognitive functions, NSS and mood symptoms in a group of euthymic patients with bipolar disorder and a control group. The principal aim of this study was to evaluate the extent to which these domains contribute to social disability and to identify the specific links and interactions between these variables.

2. Methods

2.1. Settings and sample

Sixty patients with bipolar I disorder and 41 age- and sex-matched healthy controls were included in the current study. The exclusion criteria included a history of neurological illness, head trauma, mental retardation, a history of substance abuse (as it may influence cognitive test performance), electroconvulsive therapy in the previous 6 months, and diagnosable or self-reported visual impairment of any other cause. All patients who were diagnosed with bipolar I disorder attended the outpatient unit of Cerrahpaşa Medical Faculty Department of Psychiatry between May 2012 and October 2013. The patients were consecutively asked to consent to participate in the study. The patients were euthymic at the time of inclusion in the study. The patients who had a Hamilton Rating Scale for Depression (HAM-D) score > 8 and a Young Mania Rating Scale (YMRS) > 6 were excluded from the study (Hamilton, 1960; Young et al., 1978). The diagnosis of bipolar I disorder in these patients was established according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision (DSM-IV-TR) criteria (American Psychiatric Association (APA), 2000) after a detailed clinical examination by two consulting psychiatrists.

The study was approved by the Istanbul University Cerrahpaşa Medical Faculty Ethical Committee, and all participants provided written informed consent.

2.2. Procedures and materials

The principal author (Tuba Öcek Baş) performed the neuropsychological assessments of each participant in a single session and fixed order, and the first author was not blind to the group allocation. The tests lasted for 2 h, and breaks of 10–15 min were allowed. A battery of neurocognitive functions was designed to assess the following domains: verbal learning and memory, visual memory, and executive functions. The neurocognitive functions were evaluated with the following tests: the Rey Auditory Verbal Learning Test (RAVLT) (Rey, 1964), the Wechsler Memory Scale-Revised (WMS-R) (Wechsler, 1987) visual reproduction subscale, the Stroop Color–Word Interference Test (SCWIT) (Golden, 1978) and the Trail Making Test A (TMT-A) and Trail Making Test B (TMT-B) (Reitan, 1958).

The presence and severity of NSS were assessed using the Neurological Evaluation Scale (NES), which was originally developed by Buchanan and Heinrichs (1989). The NES measures the following four domains: sensory integration, motor coordination, sequencing of complex motor acts, and other soft signs. The assessment of NSSs was conducted by the principal author, who was trained and supervised by a psychiatrist. The evaluators administered the scale based on the original scoring instructions; thus, the items were scored 0 (no abnormality), 1 (mild but

definite impairment), or 2 (marked impairment). Two items, the suck and snout reflexes, were scored 0 (absent) or 2 (present). Fourteen items are assessed bilaterally. In the current study, the right and left scores were summed for the bilateral items. The potential range of the total score was 0–76.

The mood of the participants was assessed using the Hamilton Rating Scale for Depression (HAM-D) (Hamilton, 1960) and the Young Mania Rating Scale (YMRS) (Young et al., 1978). Life charts, graphic representations of the patients' courses of mood episodes over time, were constructed. The assessment of social disability was accomplished using the Functioning Assessment Short Test (FAST) (Rosa et al., 2007). The FAST includes 24 items that evaluate six specific areas of functioning, autonomy, occupational functioning, cognitive functions, financial status, interpersonal relations and leisure activities. Each item is scored on a 3-point Likert scale. The range of the total score is 0–72 points. Higher scores indicate a lower level of functioning.

2.3. Statistical analysis

Prior to data analysis, the data were checked for normality using analytical (Kolmogorov Smirnov/Shapiro–Wilk's tests) and visual methods (histograms and probability plots). With the exception of age, the variables were not normally distributed. The data that failed the tests of normality were subject to analysis with a Mann–Whitney U test, which was used to compare the ordinal data between the independent groups. The categorical variables were compared with a Chi-square test. The associations among the socio-demographic characteristics, illness variables, cognitive performance and NSS were explored using the Spearman correlation coefficient r. Using the median value of the FAST as the cut-off point, the patients were divided into two groups, high or low functioning. The patients with high ($n=29$) and low ($n=31$) functioning were compared regarding the total NSS, residual depressive symptoms, cognitive performance and clinical variables. The normally distributed data were compared with an independent samples t-test.

Illness variables, cognitive performance and NSS were subjected to binary logistic regression analysis to predict the level of patient functioning. To reduce the risks of false positives in the correlation analysis, a significance level of $p < 0.01$ was adopted. For the remaining analyses, statistical significance was established at $p < 0.05$. The statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 15.0 (SPSS, Inc., Chicago, IL, USA).

3. Results

3.1. Sample characteristics

The study comprised 60 patients with bipolar I disorder and 41 healthy subjects. The socio-demographic and illness-related characteristics of the participants are presented in Table 1. There was no significant difference between the groups in terms of gender, age or years of formal education. However, the groups were significantly different in terms of marital status (single–divorced/married) and occupational status (employed/unemployed). Higher rates of single/divorced ($\chi^2=6.99$, df$=1$, $p=0.008$) and unemployed individuals ($\chi^2=15.01$, df$=1$, $p=0.001$) were identified in the patient group compared with the healthy controls.

All of the patients were euthymic for a minimum of 1 month at the time of the evaluation. All patients were on medication. No significant differences were found with respect to lithium, valproate or lamotrigine use between high- and low-functioning patients. However, a significantly higher number of patients in the