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Theory of mind and facial emotion recognition in euthymic bipolar I and bipolar II disorders

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ABSTRACT

The main aim of this study was to compare patients with euthymic bipolar I (BDI) and bipolar II (BDII) disorders and healthy controls in measures of social cognition. Additional aims were to explore the association between social cognition performance with neurocognitive impairments and psychosocial functioning. Eighty one euthymic patients with BDI or BDII and 34 healthy controls were included. All subjects completed tests to assess verbal memory, attention, and executive functions. Additionally theory of mind (ToM) and facial emotion recognition measures were included. Psychosocial functioning was assessed with the GAF. Both groups of patients had lower performance than healthy controls in ToM, and a lower recognition of fear facial expression. When neurocognitive impairments and exposure to medications were controlled, performance in ToM and recognition of fear facial expression did not allow predicting if a subject was patient or healthy control. Social cognition measures not enhance variance beyond explained by neurocognitive impairments and they were not independent predictors of psychosocial functioning. Impairments in facial emotion recognition and ToM are mediated, at least partly, by attention-executive functions deficits and exposure to psychotropic medications. Likewise, social cognition measures did not contribute to variance beyond neurocognitive impairments.

1. Introduction

There is a growing body of evidence that patients with bipolar disorder (BD) have neurocognitive impairments even during euthymic periods. Verbal memory, attention, and executive function impairments are the most consistent findings (Robinson et al., 2006; Torres et al., 2007; Arts et al., 2008; Kurtz and Gerraty, 2009). Moreover, it has been showed a negative association between neurocognitive functioning and different measures of disability both in cross-sectional (Zubieta et al., 2001; Dickerson et al., 2004; Martinez-Arán et al., 2004; Martino et al., 2008) and longitudinal (Jaeger et al., 2007; Tabarés-Seisdedos et al., 2008; Martino et al., 2009) studies.

Despite that euthymic patients with BD may show impairments in neurocognitive domains, there is paucity of information about social cognition skills in this population. Social cognition refers to the mental operations underlying social interactions, which could be relatively independent from other aspects of cognition and it is not assessed by traditional neurocognitive tasks (Pinkham et al., 2003). One of the key aspects of social cognition is the ability to infer mental state (beliefs, thoughts and intentions) of others that has been conceptualized as theory of mind (ToM). The first study specifically designed to assess ToM in BD reported than both symptomatic manic and depressive patients had impairments while patients in remission had a comparable performance to healthy controls (Kerr et al., 2003). Contrarily, more recent studies in euthymic BD patients showed impairments in ToM tasks (Inoue et al., 2004; Bora et al., 2005; Olley et al., 2005; Lahera et al., 2008). More controversial findings come from studies in euthymic BD that assessed other aspects of social cognition as the ability to discriminate accurately between different facially expressed emotions. A small study reported that patients with BD type II (BDII) ($n=8$) showed greater recognition of fear than those with BD type I (BDI) (Lembke and Ketter, 2002), while Harmer et al. (2002) found a robust facilitation in the discrimination of disgusted facial expressions in patients with BD compared with matched controls. Contrarily, in a study by Venn and colleagues (2004) there were no differences in facial affect recognition between BD patients and healthy controls, although there was an evident statistical trend to lower recognition of fear among patients suggesting that the lack of significance may be the result of underpowering ($n=17$) of the study. Similarly, Bora et al. (2005) showed similar facial affect recognition of basic emotions between patients with BD and healthy controls. Finally, Bozikas et al. (2006) found in a small sample ($n=19$) of remitted BDI patients that they were restricted on the matching of facial basic emotional expressions.

These inconsistent results may be associated with methodological factors as small sample size, heterogeneous samples, and inadequate control of subclinical symptoms or IQ among others. Additionally, several issues must be elucidated regardless of social cognition in BD. First, almost all previous studies included mixed samples with major

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depressive disorder and BD (Inoue et al., 2004) or just patients with BDI (Bora et al., 2005; Olley et al., 2005; Lahera et al., 2008) because of this nowadays it is not clear if other subtypes of BD have impairments in ToM. Previous researchers found that patients with BDII had impairments in verbal memory, attention, and executive functions slightly less severe than those with BDI (Torrent et al., 2006; Simonsen et al., 2008). However, to the best of our knowledge, no previous studies explored performance of patients with BDII in ToM tasks. Furthermore, the effect of other neurocognitive impairments in ToM dysfunction is an unresolved issue. In the study by Bora et al. (2005) executive dysfunction was partly responsible of ToM deficits, while in the study by Lahera et al. (2008) sustained attention impairment was a confusion factor in the differences found in ToM according to the group (BD or healthy controls). This is a critical point to determine if social cognition impairments would be trait-markers of BD. Finally, just one previous study assessed the relationship between social cognition impairments and measures of functional outcome (Olley et al., 2005). In that study, ToM was not significantly correlated with any measure of social and occupational functioning, although the small sample size ($n=15$) might limited the statistical power of the analysis.

The aim of this study was to compare euthymic patients with BDI, BDII, and healthy controls in measures of social cognition. Taking into account methodological limitations of previous studies, we included a large sample of BDI and BDII patients meeting strict euthymia criteria, paired in several clinical and demographical variables of interest, and assessed with a quantitative measure of exposure to psychotropic medications. A second aim was to explore the influence of neurocognitive impairments in social cognition abilities. A final aim was to explore the relationship between measures of social cognition and psychosocial functioning. Based on previous studies, we hypothesize that both BDI and BDII patients would have impairments in social cognition measures and that these would be negatively influenced by neurocognitive functioning.

2. Methods

Eighty one subjects with BD (45 BDI and 36 BDII) were consecutively selected from the outpatients population of the Bipolar Disorder Program of the Favaloro University with the following inclusion criteria: age between 18 and 60 years old; diagnosis of BDI or BDII according to DSM-IV using Structured Clinical Interview for DSM-IV (SCID) (First et al., 1996); euthymic (defined by Hamilton Depression Rating Scale ≤8 and Young Mania Rating Scale ≤6) for at least 8 weeks. Exclusion criteria were: history of substance abuse, history of mental retardation, neurological disease, or any clinical condition (like hypothyroidism or diabetes) that could affect cognitive performance. Additionally, 34 healthy controls matched by age and years of education were included: these had no 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. Further details of the sample characteristics can be found in a sutdy that assessed the neurocognitive profile of patients with euthymic BDII (Martino et al., 2011). The study was approved by the Hospital Ethics Committee in accordance with the Helsinki Declaration of 1975. All subjects gave written informed consent for their participation after receiving a complete description of the study.

2.1. Clinical assessment

In addition to SCID, all subjects were evaluated with the Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960), and Young Mania Rating Scale (YMRS) (Young et al., 1978). Additional clinical information was obtained from clinical charts and direct patients interview. Psychosocial functioning was assessed with the General Assessment of Functioning (GAF) (DSM-IV). The rater was instructed to use the GAF to measure functioning and not symptoms in the last month since other measures of mood symptoms (HDRS and YMRS) were obtained as a part of the study. Exposure to antidepressants, mood stabilizers, antipsychotics, and benzodiazepines was assessed by Clinical Scale of Intensity, Frequency, and Duration of Psychopharmacological Treatment (Peralta and Cuesta, 2002). This scale provides a quantitative measure of current exposure to different groups of psychotropic medications in a 0–5 points range (0 = no medication, 1 = sporadic low dose, 2 = continue low dose; 3 = middle dose, 4 = high dose, and 5 = very high dose).

2.2. 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); and 3) Executive functions: *Semantic and Phonological Fluency* (Benton et al., 1983); and Trail Making Test part B (Reitan, 1958). Additionally, estimated premorbid IQ was calculated by the WAIS vocabulary subtest (Wechsler, 1955).

2.3. Social cognition assessment

2.3.1. Faux Pas test

(Stone et al., 1998). This ToM test consists in 10 stories in which one of the characters says something that it would be better not to say (faux pas). The text of each story is placed in front of the subject so that it may be referred to, thereby reducing the demand made on working memory. After reading the story aloud, the interviewer asks: 1) Does somebody say something that it would be better not to say?; in case of an affirmative answer 2) Who?, and 3) Why do you think he/she says so? Although the answer to question 1 is affirmative or negative, the interviewer makes a reality question to test general comprehension and memory. One point is given for each correct answer and none for the incorrect ones. Alternatively with these stories, ten control stories are read in which there are no faux pas, and the first and reality questions are asked (one point for correct answer and none for incorrect one). Once 20 histories have been read, a ToM index (IToM) can be get as follows: somebody + who + why + control histories/40 (total score ranges from 0 to 1). By the same manner a memory index can be obtained: reality question faux pas + reality question control history/20 (total score ranges from 0 to 1).

2.3.2. Reading the Mind in the Eyes test

(Baron-Cohen et al., 2001). The revised version of this task consists of the photograph of the eyes region of 36 faces. The subject is required to make a choice between four words printed at the page on which the picture appears and to choose the one that best describes what the individual on the photograph is thinking or feeling (e.g. serious, ashamed, alarmed, or bewildered). This test places no memory demands on the subject.

2.3.3. Ekman-60

(Young et al., 2002). In this test different faces appear in random order for 5 s each in the PC monitor, and subjects have to recognize facial expression of six basic emotions (anger, disgust, fear, surprise, happiness, and sadness). The test yields a score out of a maximum of 60 correct answers for recognition of all six emotions, or scores out of 10 for recognition of each basic emotion.

One experienced psychiatrist (SAS) examined clinically all subjects. All neurocognitive tests were administered by other physician (DJM) in a quiet testing room according to a standardized order.

2.3.4. Statistical analysis

The assumption of normality of each variable was analyzed with the Kolmogorov–Smirnov normality test. The three groups (BDI, BDII, and healthy controls) were compared in clinical–demographical and neurocognitive variables using analysis of variance (ANOVA) and chi squared tests as appropriate. A Tukey post hoc comparison procedure was used followed ANOVA when significant main effects were present. Social cognition variables were nonparametric in our study as in all previous studies that analyzed the assumption of normality of these variables (Lembke and Ketter, 2002; Kerr et al., 2003; Venn et al., 2004; Bora et al., 2005; Lahera et al., 2008). Therefore, these variables were analyzed using the Kruskal–Wallis analysis of variance, and Mann–Whitney test was used for comparison between each BD patient group and healthy controls. In order to decrease the risk of type I error an optional Bonferroni correction was applied. The P value of each cognitive domain was calculated by dividing 0.05 to the number of cognitive variables on that area. This method was the same procedure that was used in the largest study publicated to date about ToM in BD (Bora et al., 2005). The relationship between social cognition with clinical, neurocognitive, and functional measures was explored using Spearman correlation coefficients, with a significance level of $P<0.05$. A multiple linear regression analysis was performed to assess the effect of neurocognitive skills and clinical variables on social cognition measures.

3. Results

Clinical and demographical features of bipolar patients and healthy controls are shown in Table 1. All patients were receiving mood stabilizers at time of testing; additionally 36% were receiving antidepressants, 48% benzodiazepines, and 54% antipsychotics. Patients with BDI had higher exposure to antipsychotics than those with BDII (70.73% vs. 40.66%; $X^2=4.20$, d.f. = 1, $P=0.040$); no differences were found between patient groups in terms of exposure to other groups of psychotropic medications. Likewise, patients with BDI had higher dose of antipsychotics assessed with IFD scale than those with BDII [1.44 (1.07) vs. 0.73 (0.91) respectively; d.f. = 1; $F=8.50$; $P=0.005$]. No other differences were found between patient groups in term of doses of psychotropic medications [mood stabilizers: 3.07