

Social cognition in euthymic patients versus their biological siblings: comparability in mental state decoding and cognitive deficits

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Introduction

Recent studies on bipolar disorder (BD) have reported a deficit in social recognition and emotional deficit even in the remission period of the disorder. Given that impaired social cognition in patients with serious mental illness impacts on increased symptom severity, prolonged course of illness, higher rates of relapse, and daily functioning, characterization of the extent of these deficits is important.

Aim of the study

The aim of this study was to examine differences in social cognition in samples of euthymic patients with first-episode BD type I, their unaffected biological full siblings, and healthy participants, as well as to determine whether the between-group differences reported above were mediated by clinical characteristics in euthymic patients.

Patients and methods

The study included 90 participants: 30 euthymic male patients with first-episode BD type I diagnosed according to *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed.; 30 unaffected full siblings of the euthymic patients; and 30 healthy controls. The three groups were matched as regards age, sex, education, marital status, and employment. All participants were subjected to social cognitive assessment using the reading the mind in the eyes (*_eyes task_*), to assess the emotional aspects of theory of mind (ToM), and the ToM's pictorial story tasks.

Results

The patients and their unaffected biological full siblings were significantly impaired in social cognition relative to controls assessed using the eye task and the pictorial story task ($P < 0.001$ and < 0.0001 , respectively). Compared with unaffected siblings, patients with BD performed poorly on the emotional and cognitive tasks.

Conclusion

Our study suggests that euthymic patients with BD type I have deficits in cognitive and emotional ToM. In fact, it can be concluded that the deficits in social cognition may be endophenotypic markers of genetic vulnerability to BD type I.

Keywords:

biological siblings, euthymic bipolar disorder, social cognition

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Introduction

Bipolar disorder (BD) is a highly prevalent lifelong neuropsychiatric syndrome characterized by recurrent mood episodes [1], which often lead to debilitating clinical and functional outcomes. Overall, 30–60% of patients experience occupational impairment and social dysfunction even during interepisode euthymic states [2–7]. Therefore, psychosocial dysfunction among BD patients is not limited to symptomatic periods but may be enduring or result in sustained disability, which contributes to high personal suffering and socioeconomic costs to society [8,9]. One of the major features of bipolar patients is their problem in societal and interpersonal performances; theory of mind's (ToM) deficit is one of the effective factors in the damaged relationships of these patients. This results in their

inability in understanding other people's viewpoint [10]. In the last decade, several studies have showed an impairment of social cognition in BD, both in the symptomatic and in the euthymic phase [11–14].

Social cognition is a concept introduced to examine the underlying mechanisms of social impairment in neuropsychiatric disorders. Recent studies in BD have reported a deficit in social recognition and emotional deficit even in the remission period of the disorder [15–18]. Social cognition describes the mental operations that underlie social interactions, including perceiving, interpreting, and generating responses to the intentions, dispositions, and behaviors of others [19]. 'Theory of mind' is a crucial facet of social cognition, and can be defined as the ability to infer and predict the intentions, thoughts, desires,

intuitions, behavioral reactions, plans, and beliefs of other people [19–21] through an awareness that others have a mind with mental states, information, and motivations that may differ from one's own [22,23]. A prominent feature of BD is its significant negative impact on work-related, interpersonal, and leisure activities [24]. As ToM is so central to human life, any impairment of this cognitive capacity can only be detrimental to social functioning [25]. Given that impaired social cognition in patients with serious mental illness impacts on increased symptom severity, prolonged course of illness, higher rates of relapse, and daily functioning, characterization of the extent of these deficits is important [11,26,27]. ToM has two factors: the first is switching mental states (social perception), which is also called emotional theory mind, and the second is mental state reasoning (social recognition), also called a cognitive ToM [28]. Most of our knowledge of cognitive deficits in both BD and schizophrenia comes from studies of nonsocial cognition (e.g. attention and memory) [29,30]. However, social cognition has not been systematically examined in BD across subdomains. Social cognition can be divided as follows: low-level processes, which involve the recognition and perception of socioemotional cues, including facial expression, vocal intonation, and gestures; and high-level processes, which include inferences about the mental states of others (i.e. mental state attribution), empathy, and emotional regulation [31].

Hypothesis: we hypothesized that the performance of euthymic patients with first-episode BD type I would be impaired relative to their siblings and healthy participants.

The present study aimed to (i) examine differences in social cognition in samples of euthymic patients with first-episode BD type I, their unaffected biological full siblings, and healthy participants, as well as (ii) to determine whether there is an association between some clinical characteristics and impaired social cognition in the euthymic patients.

Setting of the study and participants

This study was conducted in the Department of Psychiatry, Psychiatry and Addiction Medicine Hospital, Cairo University Hospitals. The study was approved by the local Scientific and Ethics Committee and all participants were enrolled after obtaining written informed consent. The study included three groups: euthymic male patients with first-episode BD type I, their adult unaffected biological full siblings, and a healthy comparison group. All groups comprised 30 participants. The inclusion criteria for the participants in all three groups were as follows: male participants between 25 and 35 years of age. The 'euthymic patient' group included those with a diagnosis of BD type I of first episode according to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. Text Revision (DSM-IV TR) criteria [32] and currently in the euthymic phase. First episode was defined as the first lifetime occurrence of a manic, depressive, or mixed episode. The clinical state of the patients was determined using the Hamilton

Depression Rating Scale (HDRS; [33]) and the Young Mania Rating Scale (YMRS; [34]). Euthymic state was defined as HDRS of 7 or less; subsyndromal depression was considered between 8 and 17, and at least 18 was considered as clinical depression. The YMRS was also established into three courts: less than 6, euthymia; 7–14, subsyndromal manic symptoms; and more than 14, clinical mania [35]. The 'unaffected siblings' group included adult full biological siblings of the euthymic patients who participated in the study. The three groups were matched as regards sex, age, educational level, marital status, and employment. The Structured Clinical Interview for DSM-IV Axis I Disorders [21] was administered to all participants to confirm their diagnostic eligibility. Patients were included if they had a DSM-IV diagnosis of BD type I and excluded if they had any other psychiatric disorder (axis 1). All patients were in a euthymic phase for at least 1 month following first episode. All participants had normal or corrected-to-normal vision, and none had taken a sedative or a benzodiazepine within 12 h of testing. Unaffected siblings and healthy individuals were excluded if they had a history of schizophrenia, other psychotic disorders, BD, recurrent major depressive disorder, substance dependence disorder, or avoidant, paranoid, schizoid, schizotypal, or borderline personality disorder, based on the Structured Clinical Interview for DSM-IV Axis II Disorders [36]. Additional exclusion criteria for healthy individuals were a family history of psychotic disorder or BD among first-degree relatives based on a self-report. Additional exclusion criteria for all participants were IQ below 70, substance-use disorder, a lifetime history of loss of consciousness for more than 1 h due to head trauma, a significant neurological disorder, or deafness. The socio-demographic and clinical variables of participants recorded at baseline included sex, age, marital status, educational level, employment status, living conditions, and age at onset. For the patient group, a detailed information including bipolar subtypes, episode onset, hospitalizations, history of suicide attempts, alcohol and substance abuse, and axis I comorbidity, a family history of severe mental disorders. Pattern of medication prescribed was also collected consisting of a mood stabilizer (predominantly lithium or valproate), antipsychotics, antidepressants, and others.

Instruments

The Hamilton Depression Rating Scale [33] is a widely used scale for the assessment of depression. This scale consists of 17 items and scores can range from 0 to 50. Depression is considered to be absent if scores are below 8.

The Young Mania Rating Scale [34] is a scale used to measure the severity of mania. The scores can range from 0 to 60, and a total score below 6 is considered to be indicative of euthymic range.

The Wechsler Adult Intelligence Test [37] is a comprehensive test of cognitive ability using subscales of general knowledge, similarities, picture completion, and block design. IQ score of the four subscales was used.

Social cognitive tasks

Reading the mind in the eyes (mental state decoding) (*_eyes task_*) [38]: This test was applied to assess the emotional aspects of ToM. Participants were presented with a series of 36 photographs of the eye region of faces, both male and female. Each picture was surrounded by four words describing emotions, from which participants were required to identify the emotion that was being portrayed by the subject of the photograph.

The ToM's pictorial story tasks [39]: This task was used to assess cognitive ToM. This task includes six animation stories. The maximum score is 59; therefore, higher scores in this test are indicative of the ability of ToM [40].

Procedure

Euthymic patients with first-episode BD type I were recruited from the patients attending the psychiatry outpatient department. Similarly, for each of these euthymic patient an adult unaffected biological full sibling was enrolled. The control group was recruited from the hospital staffs who were not genetically related to the patients. All three groups were recruited by means of purposive sampling. Initially, the participants were evaluated on the selection criteria, and those who fulfilled the selection criteria were enrolled. The three groups were matched as regards age, sex, level of education, marital status, and employment.

Statistical analysis

Statistical analysis was carried out using SPSS software, version 14 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics in the form of frequencies, percentages, means, and SDs were used for studying the demographic, clinical, and neurocognitive variables. The three groups were compared using the χ^2 -test for the categorical variables and analysis of variance for continuous variables. When the frequency of the number of cases for a particular variable was less than 5 in a cell, weighted cases were used to calculate the χ^2 -value. To account for the confounders, analysis of covariance was used for computation of corrected *F* scores. The post-hoc test of Bonferroni was used for comparison of individual groups. Effect sizes of the differences in neurocognitive performance were calculated using partial η^2 scores.

Results

Demographic characteristics of the sample are presented in Table 1.

The study included three groups of participants (euthymic BD type 1 group, unaffected biological full siblings of the euthymic group, the bipolar group, and the healthy control group). There was no significant difference among the three study groups with respect to various sociodemographic variables such as age, marital status, employment status, and education level.

Table 2 shows that the mean HDRS score of the patient group was 5.03 (SD: 6.08). Similarly, the mean YMRS score was 2.54 (SD: 3). About 40% of the patients were having a positive first-degree family history of severe mental disorders. The majority of the patients with mood disorder (60%) had index manic episode, and 53% of patients had been hospitalized. Length of stay in hospital in days was 23.2 (11.6). The mean duration to reach the euthymic phase was 3.7 (1.8) months. All patients of the BD were on medications; of them, 67% were receiving antipsychotics, 40% anticonvulsants (as a mood stabilizer), ten patients (33%) were receiving antidepressants, eight (27%) patients were on long-acting antipsychotic injection, and four (13%) were receiving other medications including anticholinergic drugs.

Performance on social cognitive tasks (the emotional and cognitive components of ToM) in the three study groups are summarized in Table 3, and effect sizes are listed for the differences between groups. Notably, euthymic first-episode BD 1 patients performed significantly worse compared with their unaffected siblings and comparison participants. Scores of unaffected biological full siblings of euthymic patients were significantly lower than that of the healthy comparison participants; they showed significantly poor performance. Group effects were significant for each task (Table 3). Either euthymic patients with first-episode BD type 1 or their siblings were associated with impaired performance in the emotional component of ToM, as measured using the eyes task and the cognitive component of ToM was assessed using pictorial story task compared with health participants (Table 3). Post-hoc analysis revealed that both the euthymic bipolar disorder type 1 and their sibling group were significantly less accurate compared with healthy participants ($P < 0.0001$). Unaffected biological full sibling group of euthymic patients performed at an intermediate level between healthy participants and patients (statistically significant position, $P < 0.001$) (Table 4).

Table 1 Demographic characteristics of the participants (N=30)

	Euthymic group	Biological siblings group	Healthy control group	
Age (years) [mean (SD)]	23.2 (5.6)	24.1 (6.3)	22.9 (6.1)	$F=0.13, P=0.983$
Education (years) [mean (SD)]	10.2 (4.6)	10.4 (5.1)	11.1 (5.8)	
Marital status [<i>n</i> (%)]				$F=0.03, P=0.674$
Married	13 (34)	14 (47)	15 (50)	
Unmarried	17 (57)	16 (53)	15 (50)	
Employment				$\chi^2=0.353, P=0.027$
Employed	18 (60)	20 (67)	21 (70)	
Unemployed	12 (20)	10 (33)	9 (30)	$\chi^2=0.463, P=0.687$

Within the euthymic BD type I group, to determine whether impaired social cognition mentioned above were mediated using some clinical characteristics at index episode, we investigated symptom severity, hospitalization, time to achieve euthymic state, psychotropic drug-related factors, and family history of severe mental disorders. Eyes task performance was observed to significantly negatively correlate with depressive symptoms ($r = 0.346, P < 0.0001$) and time to fulfill euthymic criteria ($r = 0.346, P < 0.0001$). The cognitive component of ToM performance was observed to significantly negatively correlate with depressive symptoms ($r = 0.346, P < 0.0001$), hospitalization time ($r = 0.205, P < 0.001$) to achieve euthymic phase, and positive first-degree family history of severe mental disorders ($r = 0.205, P < 0.001$); no other correlations were observed.

Discussion

To the best of our knowledge, this is the first study that investigated whether euthymic male patients with first-episode BD type 1 showed significant differences from

their unaffected biological full siblings and healthy controls on measures of social cognition by applying the cognitive and emotional components of ToM. Our results indicate that euthymic patients with first-episode BD type 1 reached a significantly lower level of performance in the cognitive and emotional components of ToM compared with their unaffected full siblings and healthy individuals. The results of this study showed that with regard to the cognitive and emotional ToM tasks, unaffected siblings had significantly worse performance compared with the normal group (i.e. deficit in both aspects of ToM in unaffected siblings).

The results of this study are consistent with several previous studies [13,16,41,42]. They found that euthymic bipolar patients in cognitive ToM had lower performance compared with the normal group. Studies conducted by Kerr and colleagues found a deficit of ToM during both manic and depressive episode [43]. Disorders of ToM were also observed in patients with BD during remission [44].

Regarding unaffected siblings our findings concur with that reported in previous studies which found that in neurocognitive performance compared with the healthy controls [29,45–47]. However, our findings differ from some previous reports [48,49]. It is quite possible that the differences in the findings may be influenced by the sample size and genetic loading for bipolarity. We found an association between the cognitive and emotional components of ToM deficits and clinical characteristics in euthymic patients at index episode stat. These observations are in agreement with some previous reports [50,51].

Limitation

Some limitations of the present study should be considered while interpreting the findings: limited number of participants and lack of female participants. All study groups were recruited through purposive sampling. Our sample did not include twin-pairs and the sociodemographic data were group matched rather than case-to-case matched. Another limitation is the

Table 2 Clinical characteristics and disease course of euthymic patients

Clinical variables	
HAMD [mean (SD)]	5.03 (6.08)
YMRS	2.45 (3.00)
Family history of first-degree severe mental disorder [n (%)]	
Yes	12 (40)
No	18 (60)
First episode, type [n (%)]	
Bipolar 1 disorder (manic)	18 (60)
Bipolar 1 disorder (depression)	12 (40)
Hospitalization [n (%)]	16 (53)
Length of stay (days) [mean (SD)]	23.2 (11.6)
Time to euthymic phase months [mean (SD)]	3.7 (1.8)
Current psychotropic medication [n (%)]	
Antipsychotics	20 (67)
Anticonvulsants	12 (40)
Antidepressants	10 (33)
Long-acting antipsychotic injection	8 (27)
Others	4 (13)

HAMD, Hamilton Depression Rating Scale; YMRS, Young Mania Rating Scale.

Table 3 Performance on social cognitive tasks in euthymic bipolar 1 patients, siblings, and healthy participants (N=30)

Task	Euthymic bipolar disorder group [mean (SD)]	Unaffected biological full siblings group [mean (SD)]	Healthy group [mean (SD)]	Analysis [F (d.f.)]	P	Effect size	
						Comparison	Euthymic Siblings
The eyes test (emotional component)	14.2 (3.7)	19.3 (4.6)	26.1 (6.3)	22.62 (2, 112)	<0.001	1 < 2 < 3	0.43 1.71
The pictorial story (cognitive component)	36.2 (9.6)	45.1 (11.7)	53.2 (10.4)	9.58 (2, 119)	<0.0001	1 < 2 < 3	0.52 0.96

Table 4 Correlation between scores on social cognitive tasks and clinical characteristics in the euthymic patients

Social cognitive task	Symptom severity (depressive symptoms)	Hospitalization	Time to achieve euthymic state
The eyes test	$r = 0.346, P < 0.0001$	0.121, 0.228, 0.068, 0.057	$r = 0.346, P < 0.0001$
The pictorial story task	$r = 0.346, P < 0.0001$	$r = 0.205, P < 0.001$	$r = 0.205, P < 0.001$

potential interference of psychotropic drugs on the performance of the tests, as all patients were on pharmacological treatment. Therefore, it is suggested that in the future studies both sexes be included and structural interviews be used for determining periods.

Implications

It has been recognized for some time now that establishing a clear pattern of ToM deficits in bipolar disorder may have profound implications for the clinical management of patients. Interpersonal and sociobehavioral therapy is recommended to improve the patient's interpersonal relationships.

Conclusion

The findings of the present study suggest that some social cognitive markers can distinguish unaffected full biological siblings of euthymic patients with first-episode BD type from healthy controls. This may provide quantitative deficits, which can help in implementing remedial measures.

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Conflicts of interest

There are no conflicts of interest.

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