Research paper

Social cognition moderates the relationship between neurocognition and community functioning in bipolar disorder

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A B S T R A C T

Background: Schizophrenia (SZ) studies suggest that neurocognition predicts functional outcome and that *social* cognition mediates this relationship. Bipolar disorder (BD) patients also have cognitive, social, and functional impairments but the relationship among these factors in BD is not well established. We assessed whether social cognition modulates the influence of neurocognition on community functioning in BD, as found in SZ.
Methods: 200 BD patients and 49 healthy controls (HC) were administered and compared on a battery of tests assessing neurocognition, social cognition, and community functioning. We conducted a series of regression analyses to investigate potential mediation or moderation of social cognition on the relationship between neurocognition and community functioning.
Results: BD patients performed worse on neurocognitive domains of processing speed, attention, verbal learning, and global neurocognition. Also, BD patients performed worse on theory of mind, the social cognition composite score, and community functioning. Neurocognition did not significantly predict functional outcome in our BD sample. However, we found a moderating effect of social cognition: among patients with poor social cognition, better neurocognition was associated with better community functioning, a relationship not seen in BD patients with good social cognition.
Limitations: The study was limited by a relatively small HC group and assessing one subtype of functioning status.
Conclusions: The relationship between neurocognition and community functioning in BD may be dependent on social cognition status, implying the presence of social cognitive heterogeneity. Results may be relevant to choosing proper treatment interventions depending on the patient's social cognitive level.

1. Introduction

Bipolar disorder (BD) is characterized by chronic and recurrent affective symptomatology that negatively impacts functional outcome in at least two-thirds of patients (Sanchez-Moreno et al., 2009; Huxley and Baldessarini, 2007). Mounting evidence also suggests that BD patients present with neurocognitive dysfunction. For example, a number of meta-analyses report that BD patients perform worse on neurocognitive processing compared to healthy controls (HC), particularly on neurocognitive domains of processing speed, attention, working memory, verbal learning, and visual learning, with medium to large effect sizes (Bo et al., 2017; Tsitsipa and Fountoulakis, 2015; Mann-Wrobel et al., 2011). Furthermore, recent studies suggest that poorer neurocognition in BD may be associated with worse functional outcome, disability, and

psychosocial functioning (Depp et al., 2012; Sanchez-Moreno et al., 2009; Wingo et al., 2009; Tabarés-Seisdedos et al., 2008; Martinez-Aran et al., 2007; Robinson et al., 2006) though not always (Malhi et al., 2007; Martinez-Aran et al., 2002). These deficits appear to remain even after affective remission and pharmacological treatment (Wingo et al., 2009), indicating that they are a central component of the illness.

Likewise, schizophrenia (SZ) patients also demonstrate substantial neurocognitive impairment, deficits that have consistently been shown to contribute to their poor functional outcome (Green, 1996; Martinez-Aran et al., 2007; Tabarés-Seisdedos et al., 2008). However, recent research in SZ proposes a more complicated relationship, such that neurocognition and functioning may be mediated by social cognition (Schmidt et al., 2011). Social cognition is a multi-dimensional construct which encompasses mental processes underlying social behavior such

as: 1) emotion recognition, 2) theory of mind, 3) social perception, 4) social knowledge, and 5) causal attribution style (Ochsner, 2008). This mediation effect found in SZ patients proposes the existence of social cognitive deficits (Savla et al., 2012), which subsequently predict functioning level (Couture et al., 2006). Currently, consensus exists supporting the idea that neurocognition and social cognition are two distinct constructs that do overlap, yet contribute in a non-redundant way to functional outcome (Allen et al., 2007; Sergi et al., 2007). However, these same relationships in BD patients are not as clear. While one study demonstrated that BD patients are indistinguishable from HCs on social cognition (Lee et al., 2013), most studies have reported impaired performance on social cognition, particularly domains of emotion recognition and theory of mind in BD relative to HCs (Bora et al., 2016; Cusi et al., 2012; Samamé et al., 2012). One recent meta-analysis also demonstrated impairment in similar social cognitive domains for manic, depressed and euthymic BD patients (Samamé, 2013). Results regarding the association between social cognition and functioning in BD are mixed; while one BD study demonstrated no change in functional outcome in relation to social cognitive interventions (Lahera et al., 2013), other groups found a significant relationship between social cognition and community functioning (Caletti et al., 2013), as well as a significant relationship between emotional processing and functioning only in BD patients with a history of psychosis (Thaler et al., 2014). It remains unclear whether these social cognitive deficits in BD are due to neurocognitive dysfunction, an underlying attentional bias, and/or other confounding effects such as medications.

Aspects of social cognition, such as social knowledge and emotion recognition, have been shown to mediate the relationship between neurocognition and community functioning in SZ (Schmidt et al., 2011). *Mediation* is a theoretical model that attempts to explain the process of how or why a cause-effect relationship occurs (Baron and Kenny, 1986). Rather than a direct causal relationship between the independent and dependent variables, mediation proposes that the independent variable influences a mediator variable, which in turn, influences the dependent variable. Importantly, when the relationships between the independent-mediator and mediator-dependent variables are statistically controlled, the relationship between the independent and dependent variables is no longer significant. In other words, neurocognition, which generally predicts functioning in SZ, does so partially through underlying substrates related to social cognitive mechanisms. A similar model may also explain the influence of neurocognition on community functioning in BD, though neurocognition has not always been observed to predict functional outcome. If social cognition does not mediate the relationship of neurocognition on functioning, social cognition may still influence this relationship through moderation. *Moderation*, better known as an interaction, explains when or for whom an independent variable most strongly (or weakly) influences a dependent variable (Baron and Kenny, 1986). Here, the strength or direction of the effect that an independent variable has on the dependent variable varies as a function of the level of the moderator variable. Also, moderation is typically used when a hypothesized causal relationship is weak or not found empirically. Even if social cognition does not mediate the relationship of neurocognition on community functioning in BD, social cognition may still impact this relationship as a function of the level of social cognition observed in BD patients. To date, no studies have assessed how social cognition affects the neurocognition-functioning association in a BD sample. Understanding the potential role social cognition plays on this relationship in BD, particularly when considering proper interventions and remediation strategies, may prove fruitful in improving functional outcome.

While social cognition appears to partially mediate the association between neurocognition and community functioning in SZ, it is unknown whether and in what manner social cognition impacts this same relationship in BD. Therefore, the current study aimed to assess the potential mediation or moderation of social cognition on the neuro-cognition-functioning relationship. First, we compared BD patients and HCs on demographics, cognition, and community functioning. Next, we assessed possible mediation by conducting a series of step-wise linear regressions to assess the relationship of social cognition on the neuro-cognition-functioning relationship (Hayes, 2009). In the event of no mediation, an exploratory moderator analysis would be conducted to ascertain whether the level of social cognition differentially influenced the relationship between neurocognition and functioning in BD patients. Given commonalities (i.e. clinical, genetic, and neurobiological) between SZ and BD, we anticipated that neurocognition would predict community functioning in our BD sample, and that social cognition would at least partially mediate this relationship.

2. Methods

2.1. Participants

The sample included 200 BD patients and 49 HCs recruited from Icahn School of Medicine at Mount Sinai. All procedures were approved by the Institutional Review Board and written informed consent was obtained from all participants. Inclusion criteria were: 1) diagnosis of BD I or BD II from the Structured Clinical Interview for DSM-IV (SCID-IV) (First et al., 2002), 2) 18–65 years of age, and 3) a score <8 on the Clinician Administered Rating Scale for Mania (CARS-M) (Altman et al., 1994) and <15 on the Hamilton Rating Scale for Depression (HRSD) (Hamilton, 1960). HCs were recruited separately as presenting without evidence of an Axis I disorder. Exclusion criterion for HCs included a family history of an Axis I disorder among first-degree relatives based on self-report. Exclusion criteria for all participants included: 1) history of central nervous system trauma, neurological disorder, or attention-deficit hyperactivity disorder, 2) recent substance use/dependence disorder (past three months), 3) electroconvulsive therapy (ECT) in the past 12 months, 4) active, unstable medical problem, and 5) estimated premorbid IQ <70 (from the Wide Range Achievement Test-3rd edition [WRAT-3] reading (Wilkinson, 1993)).

2.2. Clinical measures

DSM-IV BD diagnosis (or lack of Axis I diagnosis in HCs), presence of lifetime psychotic features, length of illness in years, and psychiatric medication use were derived from the SCID-IV by highly trained clinical coordinators and postdoctoral fellows. Manic and depressive symptoms were assessed by CARS-M and HRSD, respectively.

2.3. Neurocognitive measures

We evaluated neurocognition using the MATRICS consensus cognitive battery (MCCB) (Nuechterlein and Green, 2006). The MCCB includes 10 tests measuring seven domains: 1) processing speed (brief assessment of cognition in Schizophrenia [BACS], Trail Making Test Part A, and semantic fluency), 2) attention and vigilance (continuous performance test-identical pairs [CPT-IP], 3) working memory (Weschler memory scale spatial and letter number span), 4) verbal learning (Hopkins verbal learning test-revised [HVLT-R]), 5) visual learning (brief visuospatial memory test-revised [BVMT-R]), 6) reasoning and problem-solving (neuropsychological assessment battery [NAB] Mazes subtest), and 7) social cognition (Mayer-Salovey-Caruso emotional intelligence test [MSCEIT]). Here, we replaced the HVLT-R with the California verbal learning test (CVLT), as it has demonstrated better sensitivity in detecting verbal learning difficulties, particularly in less impaired BD patients (Yatham et al., 2010). BD patient scores were standardized based upon the HCs' performance (z scores: mean = 0, SD = +/−1). Global neurocognitive composite scores were calculated as mean z-scores of MCCB domains (excepting social cognition) and CVLT, with larger scores indicating better neurocognitive performance.