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The manic phase of Bipolar disorder significantly impairs theory of mind decoding

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ABSTRACT

Bipolar disorder is associated with significant deficits in the decoding of others' mental states in comparison to healthy participants. However, differences in theory of mind decoding ability among patients in manic, depressed, and euthymic phases of bipolar disorder is currently unknown. Fifty-nine patients with bipolar I or II disorder (13 manic, 25 depressed, 20 euthymic) completed the "*Reading the Mind in the Eyes" Task* (Eyes task) and the Animals Task developed to control for non-mentalistic response demands of the Eyes Task. Patients also completed self-report and clinician-rated measures of depression, mania, and anxiety symptoms. Patients in the manic phase were significantly less accurate than those in the depressed and euthymic phases at decoding mental states in the Eyes task, and this effect was strongest for eyes of a positive or neutral valence. Further Eyes task performance was negatively correlated with the symptoms of language/thought disorder, pressured speech, and disorganized thoughts and appearance. These effects held when controlling for accuracy on the Animals task, response times, and relevant demographic and clinical covariates. Results suggest that the state of mania, and particularly psychotic symptoms that may overlap with the schizophrenia spectrum, are most strongly related to social cognitive deficits in bipolar disorder.

1. Introduction

Bipolar disorder is associated with marked deficits in social and interpersonal functioning that persist into euthymia (Sanchez-Moreno et al., 2009). Because the dysfunction associated with bipolar disorder can be so profound, it is important examine the social-cognitive mechanisms that might underlie these problems. Theory of mind (ToM) – the ability to decode and reason about others' mental states, including beliefs, desires, emotions, and intentions – forms the foundation of social cognition and, thus, is critical to successful social and interpersonal functioning (Premack and Woodruff, 1978).

There are two components of theory of mind that are distinct, but that work together to facilitate social understanding: 1) *decoding* mental states from immediately available social information (e.g., facial expression, tone of voice), and 2) *reasoning* about mental states by using knowledge about others' experiences and beliefs to understand behavior (Sabbagh, 2004). This conceptualization of ToM, and particularly the construct of ToM reasoning, is complementary to the more recent distinction between 'ToM-understanding' and 'ToM-use', which have been defined as the ability to understand others' mental states and to apply that understanding in social situations, respectively (Abu-Akel, 2003; Wang et al. 2013, Wang et al., 2015). Theory of mind 'decoding' is theorized to represent the foundational component of ToM (Sabbagh, 2004) and is the component that we sought to examine in the current study. The "Reading the mind in the eyes task" (Eyes Task; Baron-Cohen et al., 2001) is the most widely used test of theory of mind decoding in adults. This difficult task requires individuals to judge the complex mental states portrayed in pictures of the eye region of faces using a forced choice among four mental state adjectives (e.g., reflective, interested, flirtatious, bored). As such it is capable of detecting very subtle differences in social intelligence.

Deficits in ToM decoding using the Eyes task have been

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observed across a range of psychiatric conditions associated with social and interpersonal dysfunction, including autism spectrum disorder (e.g., Baron-Cohen et al., 2001), schizophrenia (e.g., Sprong et al., 2007), and unipolar major depressive disorder (e.g., Lee et al., 2005). A recent meta-analysis of 12 studies that compared patients with bipolar disorder to healthy controls using the Eyes task found a significant effect size (d=.50; Bora et al., 2016). All but one of these studies included bipolar disorder patients in the euthymic phase or with subsyndromal manic or depression symptoms. The one study that included patients in the acute phases of illness also found significant impairment in the patient group relative to healthy controls (Wiener et al., 2011). Further, overall effect sizes across all ToM tasks in the full set of 34 studies included in the meta-analysis were most robust for differences between healthy controls and those in acute manic or depressive states (d=1.32).

While differences between patients with bipolar disorder and healthy controls on ToM tasks generally, and the Eyes task in particular, are robust and well-documented, to date there has been no comparison of ToM decoding abilities across the manic, depressed, and euthymic phases of bipolar disorder. This is important because there are reasons to suspect that individuals in the manic phase of bipolar disorder may be particularly impaired in their ToM decoding skills relative to those in the depressed or euthymic phases. First, in studies of ToM *reasoning*, patients in the manic phase perform worse than those in the depressed phase of illness (Kerr et al., 2003), although this group difference has failed to reach significance in other studies using a variety of different ToM reasoning measures (Bazin et al., 2009, Wolf et al., 2010).

Second, the manic phase of bipolar disorder shares some features with the schizophrenia spectrum, including language/thought disorder (e.g., pressured speech, tangentiality, flight of ideas) and delusions of reference/grandeur, and molecular and behavioral genetic work suggests that bipolar disorder may, along with schizophrenia, form part of a spectrum of neurodevelopmental disorders (Lichtenstein et al., 2009; Van Snellenberg and de Candia, 2009). In schizophrenia, deficits in theory of mind have been specifically linked to formal thought disorder (Greig et al., 2004), and researchers have suggested that poor 'mind-reading' (i.e. difficulty decoding and reasoning about others' mental states) may actually cause pragmatic impairments in thought-language expression and comprehension (Langdon et al., 2002). Similarly, Frith (1992, 1994) noted that patients with delusions of reference show marked ToM deficits, and that their delusions occur due to a lack of ability to represent others' beliefs, emotions, and intentions. Lahera et al. (2008), however, found that a previous history of psychotic symptoms was not associated with pronounced ToM deficits in bipolar euthymic patients. Furthermore, Bora et al. (2016) did not find a significant difference in ToM deficits between bipolar disorder patients with or without a history of psychosis, leading authors to question whether or not ToM deficits are a trait-marker for psychosis (Wang et al., 2008; Mitchell and Young, 2016). However, in these two latter studies patients were either examined in the euthymic phase, or phase of illness was not taken into consideration. To the extent that patients in the *manic* phase of bipolar disorder exhibit similar symptoms to schizophrenia, we may expect similar theory of mind decoding deficits. Indeed, in a meta-analysis examining several ToM tasks, severity of manic symptoms was associated with the degree of ToM performance (Bora et al., 2016).

The primary goal of the current study was to compare ToM decoding abilities assessed with the Eyes task among patients in the manic, depressed, or euthymic states of bipolar I or II disorder. We hypothesized that patients in the manic phase would perform significantly worse than those in the depressed and euthymic phases. In contrast, consistent with previous research, we did not expect to see differences in performance between those in the depressed and euthymic phases. Further, we predicted that the deficits in performance associated with the manic phase would be specifically driven by symptoms indicating thought/language disorder and delusions. Finally, we hypothesized that the above effects would be robust to individual differences across groups in response times associated with the task and in performance on a non-mentalistic control task.

2. Methods

2.1. Participants

This study was approved by the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board and the Providence Continuing Care Center Research Review Committee. Male and female inpatients and outpatients with a current diagnosis of bipolar disorder type I or II as defined in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV; American Psychiatric Association, 1994) who were above the age of 18 (M=46.7, SD=10.0; 41% female) were referred from specialized mood disorder clinics in Kingston, Ontario. Patients with a developmental disability, substance dependence, or with a serious medical condition that might have been the cause of the mood disorder (e.g. hypothyroidism) were excluded from the study. Of the 68 participants recruited, three were excluded due to exclusionary diagnoses (schizophrenia with no BP, drug induced mania, alcohol dependence), two did not complete the full Eyes Task, and five were experiencing a mixed episode.

2.2. Measures

2.2.1. Demographic interview

This interview was conducted to query patients' sex, age, educational attainment, occupation status, and marital status. Information about age of onset of illness, number of previous bipolar episodes, and comorbid diagnoses was retrieved from patient records.

2.2.2. Mania symptom measure

Symptoms of mania were assessed with the Young Mania Rating Scale (YMRS; Young et al., 1978), an 11-item interview and observation rating scale. Higher scores indicate more severe manic symptoms. This scale has strong psychometric properties (Double, 1990). Hanwella and de Silva (2011) conducted factor analysis of the YMRS in a sample of psychiatric inpatients and extracted 3 factors after oblique rotation: (1) Irritable mania: irritability, increased motor activity/energy, disruptive-aggressive behavior; (2) elated mania: language-thought disorder, elevated mood, sexual interest; and (3) psychotic mania: thought content, appearance, sleep, speech. To address our second goal we created composite scores for each factor, which consisted of summing the scores for items in each respective factor. 'Insight' loaded highly on both factor 1 (negatively) and factor 2 (positively), and 'sleep' loaded highly on both factor 2 and factor 3. Therefore, these two items were not included in the composite scores for the current study.

2.2.3. Depression and anxiety symptom measures

Depression symptoms were assessed with the 21-item Hamilton Depression Rating Scale (HDRS-21; Hamilton, 1967) and the Beck Depression Inventory- II (BDI-II; Beck, 1996). The HDRS-21 is a clinical interview and the BDI-II is a self-report scale. Both scales are used extensively in mood disorder research and have robust psychometric properties (Rehm and O'Hara, 1985; Steer et al.,