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

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A B S T R A C T

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.

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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
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 ($d=0.50$; 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, Wolff 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-mental 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., 2000).
Symptoms of anxiety were assessed with the Beck Anxiety Inventory (BAI; Beck and Steer, 1990), a 21-item self-report questionnaire designed to measure the behavioral, cognitive, and physiological symptoms of anxiety that are separate from symptoms of depression. The BAI has good psychometric properties and is widely used as a screening tool for global anxiety in psychiatric populations. Higher scores on each scale indicate more severe symptoms.

### 2.2.4. Experimental tasks

The Reading the Mind in the Eyes Task Revised Edition (Eyes Task; Baron-Cohen et al., 2001) consists of a series of 36 black-and-white magazine photographs standardized to the same size (15 cm x 6 cm) depicting the eyes, adjusted to only show from the middle of the nose to just above the eyebrows. The task involves a forced choice of one of four adjectives (one target and three distracters) that best describes the mental state expressed in each picture. All words are equally spaced from the center of the picture and the target answer location is counterbalanced. Patients were not given feedback as to how well they performed on the Eyes Task at any point. Percent accuracy on the task was used as the dependent variable (number of items scored correctly over the total number of items multiplied by 100). Response times were also recorded. The stimuli used in the Eyes task have been classified into three emotional valence categories: positive (8 items; e.g. “Friendly”), neutral (16 items; e.g. “Reflective”), and negative (12 items; e.g. “Upset”) (Harkness et al., 2005). We conducted secondary analyses to examine whether group differences on the Eyes task varied as a function of stimulus valence.

The Animals Task was used as a control task to ensure that group differences on the Eyes Task could be attributed to selective differences in theory of mind rather than to more general differences in cognitive and/or perceptual abilities (Harkness et al., 2005). The Animals Task uses the same format as the Eyes Task, but instead depicts 12 black-and-white photos of full animals and asks the participant to choose one of four descriptive words that best describe each animal. Percent accuracy on the task was used as the dependent variable. Response times were also recorded. The Animals task controls for the surface features of the task, as well as individual differences across groups in processing speed, motivation, and executive function, and thus serves to control for individual differences in neurocognition across the three patients groups.

### 2.3. Procedure

All participants provided written informed consent. Participants completed the self-report questionnaires and a registered nurse conducted the socio-demographic and clinical interviews in one session. Participants next completed a computerized version of the Eyes and Animals Tasks that randomly combined the Animals Task and Eyes Task items into a block of 48 trials. Participants responded by pressing one of four keys (S, K, X, M) that were spatially analogous to the words displayed. Using digital versions of the Eyes and Animal Tasks allowed for the collection of response accuracy, and response time for each trial. Following the study, patients received $20 as compensation for their time.

### 3. Results

#### 3.1. Item analyses

To confirm the validity of the Eyes and Animals task items we examined whether a greater proportion of participants chose the target answer than would be expected by chance, \( p = .25 \). Multiple bonferroni-corrected binomial tests showed that on all items other than 2 on the Eyes Task and 1 on the Animal Task, significantly more participants chose the target answer than would be expected by chance (two-tailed \( p < .001 \) and \( p < .004 \) for the Eyes and Animal Tasks respectively). With these 3 items removed the Eyes Task consisted of 34 items and the Animal Task, 11 items.

#### 3.2. Preliminary analyses

For the purposes of addressing our primary goal we created a grouping variable based on patients’ scores on the HDRS-21 and YMRS (Rehm and O’Hara, 1985; Young et al., 1978): (1) Depression \((n=25)\): HDRS-21 scores of 12 or more; Mania \((n=13)\): YMRS scores of 12 or more; and Euthymia \((n=20)\): HDRS-21 and YMRS below 12. Participants who had scores of at least 12 on the HDRS-21 and the YMRS were classified as experiencing a mixed episode and were excluded from the study.

Demographic and clinical characteristics by group are presented in Tables 1 and 2. No significant differences among groups were found in terms of sex, age, education, marital status, age of first diagnosis, or presence of a comorbid diagnosis (all \( ps > .05 \)). Groups differed significantly in terms of occupational status, \( \chi^2(2) = 9.96, p = .007 \), such that more currently depressed patients were either unemployed or on disability than patients in the manic or euthymic groups. There were no group differences in the frequency of patients currently taking antipsychotic, anticonvulsant, or lithium medication (\( ps > .35 \)). However, those in the depressed phase (90%) were significantly more likely than those in the manic (54%) or euthymic (35%) phases to be taking an antidepressant. \( \chi^2(2) = 13.65, p = .001 \).

As expected given the definition of groups, the manic group scored significantly higher than the depressed or euthymic groups on the YMRS, \( F(2, 55) = 101.30, p < .001 \), and its irritable, \( F(2, 55) = 14.96, p < .001 \), elated, \( F(2, 55) = 34.95, p < .001 \), and psychotic, \( F(2, 55) = 52.38, p < .001 \), factors. The depressed group scored significantly higher on the HDRS, \( F(2, 55) = 76.28, p < .001 \), and BDI-II, \( F(2, 55) = 27.87, p < .001 \) than the manic or euthymic groups. Further, the depressed group scored significantly higher than the euthymic group on the BAI, \( F(2, 55) = 10.03, p < .001 \). Finally, groups did not differ in terms of response times on either the Eyes task or the Animals task, or on accuracy on the Animals task (\( ps > .10 \)).

Eyes task accuracy was not significantly related to sex, age, marital status, occupation status, BAI scores, or presence of a comorbid diagnosis (all \( ps > .05 \)). However, those with at most a high school education (\( M = 59, SD = .16 \)) performed significantly more poorly on the eyes task than those with at least some college (\( M = .70, SD = .16 \)) or a university degree (\( M = .77, SD = .09 \)), \( F(2, 53) = 5.62, p = .006 \). Further, eyes task performance was significantly positively related to age at first diagnosis, \( r(56) = .31, p = .02 \), such that patients with a younger age of onset had significantly poorer scores on the task. Further, eyes task accuracy was not significantly correlated with response times on the Eyes task, \( r(56) = .17, p = .20 \). However, eyes task accuracy was significantly correlated with animals task accuracy, \( r(56) = .31, p = .02 \).

The results of the primary models below were robust when education attainment, occupation status, antidepressant medication status, and BAI scores were included (results available upon request). One concern with the inclusion of individuals in the
Table 1
Demographic and clinical characteristics of the sample by group.

<table>
<thead>
<tr>
<th></th>
<th>Depressed (n=25)</th>
<th>Manic (n=13)</th>
<th>Euthymic (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>12</td>
<td>40</td>
<td>4</td>
</tr>
<tr>
<td>Male</td>
<td>13</td>
<td>60</td>
<td>9</td>
</tr>
<tr>
<td>Level of education achieved*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary school or lower</td>
<td>9</td>
<td>38</td>
<td>7</td>
</tr>
<tr>
<td>Some college or University</td>
<td>10</td>
<td>42</td>
<td>2</td>
</tr>
<tr>
<td>University degree or higher</td>
<td>5</td>
<td>21</td>
<td>3</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>4</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td>Unemployed/disability</td>
<td>21</td>
<td>84</td>
<td>6</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never married</td>
<td>6</td>
<td>24</td>
<td>5</td>
</tr>
<tr>
<td>Separated/Divorced</td>
<td>10</td>
<td>40</td>
<td>4</td>
</tr>
<tr>
<td>Married/common-law</td>
<td>8</td>
<td>32</td>
<td>4</td>
</tr>
<tr>
<td>Comorbidity*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>8</td>
<td>38</td>
<td>7</td>
</tr>
<tr>
<td>Yes</td>
<td>13</td>
<td>62</td>
<td>6</td>
</tr>
<tr>
<td>Substance use</td>
<td>5</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>ADD</td>
<td>2</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>PTSD</td>
<td>3</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>SAD</td>
<td>1</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>OCD</td>
<td>1</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>GAD</td>
<td>7</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>2</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Schizoaffective disorder</td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Age at first diagnosis</td>
<td>46.96</td>
<td>8.19</td>
<td>47.69</td>
</tr>
</tbody>
</table>

Note: * data was missing for 4 patients; ** data was missing for 4 patients; ADD = attention deficit disorder; PTSD = post-traumatic stress disorder; SAD = social anxiety disorder; OCD = obsessive compulsive disorder; GAD = generalized anxiety disorder.

Table 2
Means and standard deviations of study measures by group.

<table>
<thead>
<tr>
<th></th>
<th>Depressed (n=25)</th>
<th>Manic (n=13)</th>
<th>Euthymic (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
</tr>
<tr>
<td>YMRS</td>
<td>3.36b</td>
<td>3.04</td>
<td>17.38a</td>
</tr>
<tr>
<td>Irritable mania</td>
<td>1.92b</td>
<td>1.44</td>
<td>4.92a</td>
</tr>
<tr>
<td>Elated mania</td>
<td>.83b</td>
<td>1.13</td>
<td>4.62a</td>
</tr>
<tr>
<td>Psychotic mania</td>
<td>.33b</td>
<td>1.09</td>
<td>5.69a</td>
</tr>
<tr>
<td>HDRS</td>
<td>17.08b</td>
<td>4.34</td>
<td>5.38b</td>
</tr>
<tr>
<td>BDI</td>
<td>30.39b</td>
<td>12.25</td>
<td>11.85b</td>
</tr>
<tr>
<td>BAI</td>
<td>19.01b</td>
<td>11.35</td>
<td>11.69</td>
</tr>
<tr>
<td>Eyes task accuracy (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eyes task response time (ms)</td>
<td>8836.48</td>
<td>3712.83</td>
<td>7212.15</td>
</tr>
<tr>
<td>Animals task accuracy (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Animals task response time (ms)</td>
<td>77.33</td>
<td>14.16</td>
<td>66.35</td>
</tr>
<tr>
<td></td>
<td>8507.74</td>
<td>3712.83</td>
<td>6632.60</td>
</tr>
</tbody>
</table>

Note: Superscript differences between means are significant at p < .05; ms = milliseconds; means for Eyes task accuracy are estimated marginal means controlling for Animals task accuracy and age at first diagnosis.

3.3. Main analyses: mood state and eyes task accuracy

An analysis of covariance (ANCOVA) was conducted with mood state (depressed, euthymic, manic) as the between-subject variable and average Eyes Task score as the dependent variable. Animals task accuracy and age at first diagnosis were included as covariates for the sake of parsimony. Therefore, only Animals task accuracy and age at first diagnosis were included as covariates for the sake of parsimony.

3.4. Eyes task accuracy and mania symptoms

A linear regression was conducted with Eyes task accuracy as the dependent variable and scores on the three symptom factors of the YMRS entered simultaneously as predictors. The overall model was significant, R² = .21, F(3, 53) = 4.82, p = .005, and was driven by the psychotic mania factor, β = .64, t(56) = 2.92, p = .005. More specifically, poorer Eyes task accuracy scores were significantly correlated with higher scores on the YMRS items of speech, r(56) = -.42, p = .001, thought content, r(56) = -.33, p = .01, appearance r(56) = -.31, p = .02, and language-thought disorder r(56) = -.29, p = .03 (all other symptoms, p > .05). The results of these analyses held when controlling for animal task accuracy and age of first diagnosis (results available upon request).
3.5. Secondary analyses: Mood state and the valence of mental states

To determine whether the relation of mood state and accuracy on the Eyes task was specific to eyes stimuli of positive, negative, or neutral valence we conducted a mixed model 3 (valence: positive, negative, neutral) X 3 (mood state: manic, euthymic, depressed) Analysis of Covariance (ANCOVA). As above, Animals task accuracy and age of first diagnosis were included as covariates. The multivariate valence by group effect reached significance, Wilks’ $\lambda = .86$, $F(4, 104) = 2.10$, $p = .07$. Follow-up univariate analyses revealed group differences on the positive, $F(2, 53) = 3.86$, $p = .03$, $\eta^2 = .13$, and neutral, $F(2, 53) = 5.04$, $p = .01$, $\eta^2 = .16$, but not negative, $F(2, 53) = 2.02$, $p = .14$, $\eta^2 = .07$, eyes. Manic patients were significantly less accurate than the euthymic group on the positive (p = .02) and neutral eyes (p = .008), and less accurate than the depressed group on the positive eyes as a trend (p = .06) and the neutral eyes (p = .003). The depressed and euthymic groups again did not differ (all ps > .15).

4. Discussion

To our knowledge this is the first study to examine ToM decoding abilities in patients with bipolar disorder across the manic, depressed, and euthymic phases of illness. Patients in the manic phase were significantly less accurate at decoding the subtle social features of eye expressions than those in either the depressed or euthymic phases, and this difference was driven by the disorganized speech and appearance, language/thought disorder, and delusional symptoms of mania. Importantly, there were no group differences in response time, and group accuracy differences were robust when controlling for response times and for performance on a non-mentalistic control task. As such, the current results are consistent with studies of ToM reasoning suggesting the manic phase of the bipolar illness is associated with the greatest deficits in social cognition (see Bora et al. (2016)) and they provide a novel extension of this conclusion to theory of mind decoding. Further, the current results suggest that deficits in ToM decoding within the bipolar illness are strongest to the extent that the bipolar presentation overlaps with features of schizophrenia, consistent with the spectrum approach proposed by Frith (1992), Lichtenstein et al. (2009), and Van Snellenberg and de Candia (2009). These results, taken together, highlight the importance of considering phase of illness when examining the nature of social cognitive deficits in bipolar disorder.

The current results suggest that the manic state may confer additional social-cognitive dysfunction that overlays the deficit associated with the bipolar illness generally. Future longitudinal studies that chart the within-individual changes in ToM accuracy across phases of the illness are required to fully test this hypothesis. Nevertheless, our secondary analyses suggest a possible target for this state deficit, located in the specific symptoms of language/thought disorder, pressured rate and tangentiality of speech, delusional thought content, and disorganized appearance. It is intriguing to note that these are the symptoms of mania that most closely map onto the positive symptoms of the schizophrenia spectrum. Patients with bipolar disorder have deficits in cognitive and social functioning that are as severe as those of patients with schizophrenia (e.g., Dickerson et al., 2001). Further functional deficits in bipolar disorder are more severe in the manic/hypomanic phases than in the depressed or euthymic phases, and mania symptoms correlate significantly with level of functional impairment (Henry et al., 2012). Patients in the manic phase also perform significantly worse than those in the depressed or euthymic phases on tests of executive function (Ryan et al., 2012), which is a neurocognitive domain that has found to be critical to scaffolding theory of mind ability (Sabbagh et al., 2006). As noted above, geneticists have recently suggested that bipolar disorder may be part of a spectrum of neurodevelopmental and affective disorders ranging from autism spectrum disorder to schizophrenia (Cradock et al., 2009). We suggest that an intriguing area for future research is the investigation of deficits in social cognition, and particularly the foundational skill of decoding others’ mental states, as a transdiagnostic endophenotype that may in part underlie this spectrum.

Deficits in the manic group relative to the depressed and euthymic groups were specific to eyes of positive and neutral valence. These results are surprising given the salience of positive stimuli for patients in acute phases of mania (e.g., García-Blanco et al., 2013). In the related field of facial emotion recognition, deficits in recognizing facial expressions of happiness have been found in bipolar patients relative to healthy controls (see Samamé, 2013 for a review). However, in these studies bipolar patients also have difficulty labeling expressions of sadness and other negative emotions. It is possible that deficits across the range of emotion valence in these previous studies can be accounted for by the failure to analyze separately acute manic versus depressed states. As the current study is the first to examine accuracy in mental state decoding by valence across the phases of the bipolar illness these results should be considered preliminary and are in need of replication.

4.1. Study limitations

The current results should be interpreted in the context of the following limitations. First, the sample size, and particularly the size of the mania group, was small and, thus, future studies with larger samples are required to confirm the generalizability of the current results. Nevertheless, the sizes of our groups are in line with those reported in previous studies of bipolar disorder (see Bora et al. (2016)). Second, while we did not employ a healthy control group we note that the deficits in ToM in bipolar disorder relative to healthy controls have been well-established through meta-analysis across a range of ToM reasoning tasks, as well as the Eyes ToM decoding task used here (Bora et al., 2016). Further, the purpose of the current study was not to provide a further replication of this effect, but was to examine differences across phases of the bipolar illness. Previous studies using the Eyes task have generally reported mean accuracy rates for healthy community controls ranging from 73 to 80% (e.g., Baron-Cohen et al., 2001; Donohoe et al., 2012; Lee et al., 2005; Purcell et al., 2013; Thaler et al., 2013).

Third, we examined only one component of ToM (ToM decoding) with only one task (Eyes task) that assesses only the modality of facial expression. Therefore, the relation of phase of illness in bipolar disorder to other components of ToM (ToM reasoning and ToM-use) and across other modalities of ToM decoding (tone of voice, body posture) is an important area of future research. Relatedly, it will be important for future research to clarify whether differences across the phases on bipolar disorder in ToM decoding using the Eyes task are robust when controlling for individual differences across the manic, depressed, and euthymic phases in basic face and emotion processing. Finally, the cross-sectional design of this study does not permit us to draw conclusions regarding within-person changes in ToM decoding performance across changes in the phase of illness. Therefore, future longitudinal studies that follow patients through episodes of mania, depression, and into remission are required.

4.2. Conclusions and directions for future research

To our knowledge this is the first study to find evidence for
significant impairment in the foundational social-cognitive skill of theory of mind decoding in patients in the manic phase relative to those in the depressed and euthymic phases of bipolar disorder. This is also the first study to specifically link the psychotic symptoms of mania to theory of mind impairment. Future studies are needed to (a) clarify whether differences across the phases of the bipolar disorder are seen within individuals, (b) investigate the functional link between psychotic and thought disorder symptoms and ToM decoding impairment, and (c) examine the relation of ToM decoding impairment and resulting social and interpersonal dysfunction across phases of the bipolar disorder. Future work building on the results of the current study could inform adjunctive social-cognitive remediation interventions in bipolar disorder that have the potential to alleviate the real-world relationship difficulties experienced by patients with bipolar disorder.

References