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Characterization and Interrelationships of Theory of Mind, Socially Competitive Emotions and Affective Empathy in Bipolar Disorder

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Title: Characterization and Interrelationships of Theory of Mind, Socially Competitive Emotions and Affective Empathy in Bipolar Disorder

ABSTRACT

Objective: Evidence shows impaired Theory of Mind (ToM) in patients with bipolar disorder (BD), yet research examining its cognitive and affective components simultaneously is sparse. Moreover, recognition of socially competitive 'fortune of others' emotions (e.g. envy/gloat) may be related to ToM, but has not been assessed in BD. Finally, if and how ToM and 'fortune of others' emotions relate to affective empathy in BD is currently unclear. This study aimed to address these points.

Methods: 64 BD patients and 34 healthy controls completed the Yoni task, a visual task assessing first- and second-order cognitive and affective ToM as well as 'fortune of others' emotions. The Toronto Empathy Questionnaire was used to assess self-reported affective empathy.

Results: Patients with BD showed no deficits in cognitive and affective ToM or recognition of 'fortune of others' emotions. The ability to infer 'fortune of others' emotions correlated with several ToM measures, indicating that these functions are part of the same system. Patients with BD reported similar levels of affective empathy to healthy controls, and this was not related to ToM or 'fortune of others' emotions, suggesting that affective empathy represents a separate social domain.

Conclusions: These findings highlight areas of spared social functioning in BD, which may be utilized in therapeutic strategies.

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Keywords: Social cognition, mentalizing , empathic abilities, mood disorder

INTRODUCTION

A substantial proportion of individuals with bipolar disorder (BD) experience cognitive deficits, which are known to contribute to real-world functional disability (Bowie et al., 2010; Van Rheenen et al., 2020a). These deficits occur in several domains, including social cognition (Miskowiak et al., 2019; Van Rheenen et al., 2019). In BD, social cognition may be partially independent of general cognition, with some evidence indicating that social cognition moderates the relationship between general cognition and functioning in patients with the illness (Ospina et al., 2018; Van Rheenen et al., 2014). These data thus highlight social cognitive deficits as an important component of BD's neuropsychological profile. Relevantly, current evidence suggests that social cognitive deficits in BD are quite subtle, particularly during the euthymic phase (Samamé et al., 2015; Van Rheenen and Rossell, 2014). Since it is known that subjective and objective reporting of cognitive functioning do not necessarily correspond (Burdick et al., 2005; Demant et al., 2015), social cognitive deficits may thus exist in patients with BD irrespective of self-report and may subtly contribute to the known difficulties many patients experience in terms of psychosocial functioning (Coryell et al., 1993; MacQueen et al., 2001).

Theory of Mind (ToM) is an important component of social cognition that refers to the ability to attribute mental states (beliefs, intentions and desires) to oneself and others (Povinelli and Preuss, 1995; Premack and Woodruff, 1978). It is a multifaceted construct consisting of several distinct components (Bora et al., 2016), including the capacity to a) understand the knowledge and beliefs of others (cognitive ToM), and b) understand the emotions of others (affective ToM) (Bodden et al., 2013; Bora et al., 2016; Shamay-Tsoory et al., 2007a). The ability to decode social cues in order to infer others' thoughts and emotions in social contexts is crucial in predicting the actions of others and facilitating prosocial behaviors (Van Rheenen et al., 2019). These skills are essential to social and functional success, which are widely reported as lacking in BD even beyond the long-term resolution of clinical symptoms (Coryell et al., 1993; Dickerson et al., 2001; Greenberg et al., 2014; MacQueen et al., 2001; Pope et al., 2007).

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Several existing studies indicate impairments of ToM in BD (Bora et al., 2016; Rossell and Van Rheenen, 2013; Samamé et al., 2012; Van Rheenen and Rossell, 2013), although there are exceptions (Caletti et al., 2013; Dalkner et al., 2019; Feyerabend et al., 2018; Haag et al., 2016; Purcell et al., 2013). These impairments have been reported in both cognitive and affective domains. However, the majority of the research has examined the two separately using different tasks, which has the potential to increase motivational/fatigue-related deficits that may confound findings. Studies examining cognitive and affective ToM in BD patients in the same task generally indicate impairments in the former, but not the latter (Andrews et al., 2016; Montag et al., 2010; Shamay-Tsoory et al., 2009; Wang et al., 2018).

The Yoni task was specifically designed to capture both cognitive and affective aspects of ToM in a single experiment (Shamay-Tsoory and Aharon-Peretz, 2007). An advantage of this visual task is that it requires minimal language and working memory demands and further enables the distinction between first-order (understanding what someone is thinking or feeling) and second-order ToM (understanding what someone thinks or feels about what someone else is thinking or feeling) (Shamay-Tsoory and Aharon-Peretz, 2007), thus providing the opportunity to deconstruct the multifaceted construct of ToM into specific components. Only two small studies have examined performance on the Yoni task in BD patients (Andrews et al., 2016; Wang et al., 2018). Both studies reported intact first-order ToM, and second-order affective ToM, whereas second-order cognitive ToM was significantly impaired (Andrews et al., 2016; Wang et al., 2018). Additionally, performance on the cognitive components of the Yoni task has been associated with hypomanic traits in males in the general population, with higher scores on the Hypomanic Personality Scale predicting lower ToM performance (Terrien et al., 2014). Together these studies tentatively suggest that simple ToM, as assessed with the Yoni task, is spared in BD, and that the deficits observed in more complex ToM is due to difficulties in the ability to infer others' knowledge and beliefs, rather than their feeling states.

One version of the Yoni task includes an additional test assessing the ability to make inferences about socially competitive, so-called *'*fortune of others*'* emotions. These comprise 'gloating', 'envy' and 'identifying with someone', which are complex emotional states predominantly experienced in social situations. They may therefore be related to ToM (Shamay-Tsoory, 2008). Inferences about these complex emotions is thought to be mediated by the ventromedial prefrontal cortex, a brain region that

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is consistently implicated in ToM and also BD generally (Furlong et al., 2021; Phillips et al., 2008; Shamay-Tsoory et al., 2007b). Moreover, the ability to recognize these 'fortune of others' emotions has been found to correlate with ToM performance on the Yoni task specifically (Shamay-Tsoory, 2008; Shamay-Tsoory et al., 2007b). To the best of our knowledge, recognition of 'fortune of others' emotions has not been assessed in patients with BD. However, it is plausible that this subdomain is of relevance to BD given both its overlap with ToM and dependence on the ventromedial prefrontal cortex (Ha et al., 2009; Hiser and Koenigs, 2018).

Empathy, another important aspect of social cognition, can likewise be divided into cognitive and affective components (Dvash and Shamay-Tsoory, 2014; Kanske et al., 2016). Empathy is also related to psychosocial functioning and successful social communication and interactions (Cusi et al., 2010; Seidel et al., 2012). Despite sparse research attention, some preliminary work shows that BD patients have impaired cognitive empathy, yet intact or even superior affective empathy relative to controls (Bodnar & Rybakowski, 2017; Seidel et al., 2012; Shamay-Tsoory et al., 2009). This latter finding is unsurprising given that awareness of one's own emotions - a prerequisite for the embodiment of another's - does not differ between BD patients and controls (Becerra et al., 2013; Van Rheenen et al., 2020b, 2015). Cognitive empathy is conceptually the same as ToM, in that it requires the capacity to understand another's thoughts, knowledge or emotions. In contrast, affective empathy refers to the ability to sense or feel other people's emotions (Dvash and Shamay-Tsoory, 2014; Shamay-Tsoory et al., 2009). Performance on the Yoni task has been found to correlate with responses on an affective empathy questionnaire in patients with acquired brain lesions (Shamay-Tsoory and Aharon-Peretz, 2007). While this correlation suggests overlap between ToM and affective empathy, other evidence points to a dissociation between these abilities (Kanske et al., 2016). The relationship between ToM and affective empathy in patients with BD is currently unclear. This is important to clarify however, because knowledge about whether there is a general system underlying social understanding in BD, as opposed to one that is modular, is relevant to the development of social cognitive treatments.

To improve our characterization of the social cognitive profile in BD, a better understanding of ToM, complex emotion recognition, affective empathy, and their inter-relationships is needed. Specifically, detailed knowledge about these components of social cognition in BD could increase our understanding of the underlying pathological processes and potentially pinpoint important targets for treatment. Thus, the aims of the current study were to examine; 1) first- and second-order cognitive and

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affective ToM; 2) the ability to infer complex 'fortune of others' emotions, and 3) affective empathy in patients with BD compared to controls. Based on the current literature, we hypothesized that first-order cognitive and affective ToM as well as second-order affective ToM would be spared, whereas second-order cognitive ToM would be impaired in BD patients. Moreover, we expected some impairments in recognition of 'fortune of others' emotions, but self-reported affective empathy levels similar to controls. A further exploratory question pertained to the presence and extent of inter-relationships between these sub-components of social cognition themselves, and also in relation to clinical measures in the BD group.

METHODS

The study was approved by the local Human Research Ethics Committee, and written informed consent was obtained from all participants.

Participants

A total of 64 stable outpatients with BD (BD I, n = 60; BD II, n = 4) and 34 healthy controls (HC) participated in the study (age 18-60). Participants were recruited as part of a larger neuroimaging study, using general advertisements, online websites and social media, with the BD patients also being recruited through community support groups and databases of participants held by the senior author. BD diagnoses were confirmed using the Mini International Neuropsychiatric Interview (MINI) (Lecrubier et al., 1997) according to DSM-IV-TR criteria (American Psychiatric Association, 2000). At the time of testing, no BD participant met criteria for a current mood episode. The majority of patients (n = 52) were considered affectively stable, as defined by scores of $\leq$12 on the Montgomery Asberg Depression Rating Scale (MADRS) (Davidson et al., 1986), and $\leq$8 on the Young Mania Rating Scale (YMRS) (Young et al., 1978); 45 patients also met strict criteria for euthymia defined as $\leq$8 on MADRS, and $\leq$8 on YMRS.

Exclusion criteria included: neurological/neurodegenerative disease, a history of severe head injury (loss of consciousness), hearing or visual impairments, pregnancy, language difficulties, a history of habitual drug use or dependence in the past three months prior to participation, and significant medication change in the two months prior to study inclusion. Further exclusion criteria for

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the HC group included: psychiatric illness (corroborated using MINI), family history of mood/psychiatric disorders, or current psychopharmacological medication/psychiatric care.

Measures

Descriptive measures: Information regarding medication use and dosage, age of onset, age at diagnosis, number of hospitalizations, psychosis history, and number of manic and depressive episodes were collected by self-report. Premorbid intelligence (IQ) was estimated using the Wechsler Test of Adult Reading (WTAR) (Wechsler, 2001) (see Table 1).

Theory of mind and inferring *'fortune of others'* emotions were assessed using the Yoni task (Shamay-Tsoory, 2008). This is a computerized test programmed using E-prime (the task was downloaded from https://sites.google.com/edu.haifa.ac.il/sans/lab-tasks). Participants are shown a cartoon outline of a face (called Yoni) in the middle of the screen and asked to make judgements about his mental state based on verbal cues, facial expressions or eye gaze cues. Each corner of the screen contains a picture (either objects or faces) and the participant must point to the one Yoni is referring to, based on a sentence at the top of the screen (See Figure 1 and 2 in Shamay-Tsoory (2008)). The participants are instructed to respond as fast as possible.

The Yoni task measures first and second-order ToM in two blocks. The first-order ToM block comprises 12 cognitive trials (Yoni is thinking of _), 12 affective trials (Yoni loves _) and a control condition, including 8 physical items without the mentalizing component (Yoni is close to _). The second-order ToM block comprises 12 cognitive trials (Yoni is thinking about the flower that _ wants), 12 affective trials (Yoni loves the animal that _ does not love) and 6 physical control trials (Yoni has the toy that ___ has). In some trials, Yoni´s facial expression is neutral and in some it is emotionally loaded.

The additional *'fortune of others'* block is inbuilt into the Yoni task. Within this, there are three conditions in which participants are asked to identify the character that Yoni is gloating over (6 trials), envies (6 trials), or identifies with (6 trials), as well as a control condition requiring Yoni's facial expression to be matched to other characters (physical #2, 6 trials). In all 'fortune of others' conditions, a combination of Yoni and the other characters´ facial expressions must be used to make the judgment.

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Participants completed the task on a Lenovo computer (14″). Responses were made with a mouse click and the cursor was returned to the center of the screen after each response.

Affective empathy was measured using the Toronto Empathy Questionnaire (TEQ; Sprens et al., 2009). The TEQ is a short, self-report questionnaire with good psychometric properties that conceptualizes empathy as a primarily affective process (Sprens et al., 2009). It entails 16 statements, which participants are asked to rate how frequently they feel or act in the manner described. Responses are scored as "Never", "Rarely", "Sometimes", "Often", and "Always". Half of the items are positively worded, and half are negatively worded with reverse scoring. Scores are summarized into a total TEQ score, with higher scores indicative of higher affective empathy levels.

Statistical analyses

All statistical analyses were performed using SPSS (version 25.0, SPSS Inc.). Initial data checking indicated that YMRS, MADRS, WTAR and Yoni data were not normally distributed according to the Kolmogorov–Smirnov test, thus non-parametric tests were applied. Group differences in age, sex, estimated premorbid IQ (WTAR), and level of functioning were analyzed using t-tests, Chi-square tests and Mann-Whitney U. Given a significant group difference in WTAR scores ($U = 557.0$, $p < .001$, $r = -0.35$), which could affect the measures of interest given evidence of an association between ToM and cognitive ability (Olley et al., 2005), we further assessed whether the WTAR was associated with the Yoni data or affective empathy scores using Spearman's Rho correlations. As no significant correlations were evident between these data (all r´s < .21, all p´s > .038), WTAR scores were not covaried in subsequent analyses.

Initially, group differences between BD patients and controls on the Yoni task and TEQ were examined using the Mann-Whitney U test. Effect sizes were calculated as $r = Z/\sqrt{N}$, with r values of 0.1, 0.3, and 0.5 indicative of small, medium and large effects respectively (Fritz et al., 2012). As a precautionary measure, one-sample t-tests were used to identify if there were any ceiling effects in the accuracy data of all conditions of the Yoni task. The TEQ total score was normally distributed and examined using an independent t-test and Cohen's d. Intercorrelations between the Yoni data and the TEQ were examined using Spearman's Rho in the full sample and also in the BD group itself. Further correlations examining the association between the variables of interest and clinical variables were

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conducted. Finally, effects of medications were explored. These latter two analyses were conducted in the BD sample only.

Re-analysis of all statistical tests comparing only those BD patients that were strictly euthymic to HCs was also conducted to examine the effect of current mood symptoms on the results. As the results of the re-analyses remained unchanged when case-control analyses were restricted to euthymic BD patients, for brevity only the analyses in the full BD sample are presented below (see supplementary material for the average Yoni performance in euthymic patients (**Table S1**)).

For each type of analysis, Bonferroni correction was applied to the alpha level to account for multiple comparisons (see supplementary material for more details regarding the number of tests used to calculate the Bonferroni corrected alpha value for each type of analysis). We also applied an alpha of $p < .01$ to verify our findings using a less stringent statistical correction method.

RESULTS

Demographic and clinical variables are presented in **Table 1**. The BD and HC groups were well matched, with no significant differences in age ($t(1, 95) = 0.529$, $p = .598$) or sex ($\chi^2 (1) = 0.492$, $p = .483$).

[INSERT TABLE 1 HERE]

Yoni task and TEQ

Mean accuracy and reaction time (RT) data from all conditions within all blocks of the Yoni task and the TEQ are presented in **Table 2**. While no ceiling effects were evident (all ceiling effect results survived the Bonferroni-adjusted alpha level of $p < .005$; all t's > -3.08, all p´s < .003), no results from the group difference analyses were significant using the Bonferroni-adjusted alpha level of $p < .002$ (.05/21) or even a less stringent alpha value of $p < .01$. Details are provided below.

First-order ToM: There were no significant differences between BD patients and HCs in accuracy scores in the cognitive ($U = 938.5$ $p = .112$, $r = -0.16$), affective ($U = 1048.5$, $p = .628$, $r = -0.05$) or physical ($U = 965.5$, $p = .210$, $r = -0.13$) conditions. No RT differences were evident in the affective ($U = 912.0$, $p = .189$, $r = -0.13$), or physical condition ($U = 894.0$, $p = .148$, $r = -0.15$). We did observe a significant difference in RT in the cognitive condition, with patients responding faster than

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controls using a less stringent alpha value of $p < .01$, however this did not survive Bonferroni correction ($U = 702.0$, $p = .004$, $r = -0.29$). Effect sizes were in the small range.

Second-order ToM: No significant accuracy differences were observed between BD patients and HCs in the affective ($U = 889.5$, $p = .131$ $r = -0.15$), cognitive ($U = 837.5$, $p = .058$, $r = -0.19$) or physical ($U = 1034.0$, $p = .651$ $r = -0.05$) conditions. There were no significant RT differences in any condition (cognitive: $U = 1012.0$, $p = .571$, $r = -0.06$, affective: $U = 1005.0$, $p = .536$, $r = -0.06$, physical: $U = 997.0$, $p = .497$, $r = -0.07$). Effect sizes were generally small, with the largest effect observed for second-order cognitive accuracy.

'Fortune of others' emotions: There were no significant group differences in accuracy in the gloating ($U = 1059.5$, $p = .823$, $r = -0.02$), envy ($U = 901.5$, $p = .134$, $r = -0.15$), identification ($U = 1050.0$, $p = .750$, $r = -0.03$) or physical #2 ($U = 1065.0$, $p = .847$, $r = -0.02$) conditions, nor were there differences in RT in any of these conditions (gloating: $U = 1001.0$ $p = .516$, $r = -0.07$, envy: $U = 1040.0$, $p = .720$, $r = -0.04$, identification: $U = 977.0$, $p = .407$, $r = -0.08$, physical #2: $U = 1001.0$, $p = .516$, $r = -0.07$). Effect sizes were in the small range, with the largest effect size observed for envy accuracy.

Affective empathy: There were no significant differences between BD and HCs on the TEQ total score ($t(1, 92) = -0.883$, $p = .379$, $d = -0.19$). The size of the case-control effect was small.

[INSERT TABLE 2 HERE]

Associations between variables

Correlations between Yoni task data and TEQ scores: In the full sample, envy accuracy correlated significantly with first-order affective ($r_s(96) = .346$, $p = .0004$), second-order cognitive, ($r_s(96) = .372$, $p = .0002$) and second-order affective accuracy ($r_s(96) = .463$, $p < .0001$), whereas gloat accuracy only correlated significantly with second-order affective accuracy ($r_s(96) = .359$, $p = .0003$), using a Bonferroni-adjusted alpha level of $p < .007$. Identification accuracy did not correlate with any

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of the ToM measures (all *r's* < .161, all *p's* > .112) (**Table 3**). When the sample was restricted to BD patients, envy accuracy still correlated with second-order affective accuracy, while gloat accuracy correlated significantly with both second-order cognitive and second-order affective accuracy (**Supplementary Table S2**). Most of the RT variables from the ToM conditions correlated with the RT for 'fortune of others' emotion conditions both in the full sample (**Table 3**) and in BD patients only (**Supplementary Table S2**), indicating that fast responders were fast on most trials.

The TEQ total score did not correlate with Yoni task accuracy data from any of the conditions within first-order ToM, second-order ToM or 'fortune of others' emotions after Bonferroni corrections either in the full sample (all r´s < .126 , all p´s > .227) (**Table 3**) or in BD patients only (all r´s < -.320 , all p´s > .010) (**Supplementary Table S2**). The TEQ total score was correlated with RT from the envy condition ($r_s(92) = -.369$, p = .0003) in the full sample (**Table 3**).

[INSERT TABLE 3]

Associations between Yoni task data, TEQ scores, clinical measures and medications in the BD group: There were no significant associations between accuracy in Yoni task data and mood symptoms measured by the MADRS and YMRS in the BD patient group (all r´s < -.184, all p´s > .145). Performance on the Yoni task did not correlate with age of onset (all r´s < -.195, all p´s > .150), age at diagnosis (all r´s < -.212, all p´s > .107), number of hospitalizations (all r´s < -.199, all p´s > .127), number of manic episodes (all r´s < .257, all p´s > .045) or number of depressive episodes (all r´s < .201, all p´s > .123). Performance on the Yoni task did not correlate with mean lithium dose in the BD sample (all r´s < .270, all p´s > .236). Additionally, there were no significant differences (after Bonferroni correction) in Yoni performance between unmedicated patients, patients using typical antipsychotics, atypical antipsychotics, mood stabilizers, antidepressants or a combination of medication types (all X^2's < 11.51, all p*'s* > .042). Finally, there were no significant differences between patients with a history of psychosis (n=38) and patients without a history of psychosis (n=25) on either ToM or empathy measures (all U^2's > 410.0, all *p's* > .150).

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DISCUSSION

The current study investigated ToM in a sample of patients with BD using a task designed to disentangle cognitive and affective ToM in the context of first-order and second-order ToM abilities. As expected, BD patients performed at the same level as HC's with regard to both cognitive and affective first-order ToM, consistent with the previous literature using the Yoni task in BD patients (Andrews et al., 2016; Wang et al., 2018). Also consistent with the two previous studies was the observation of no group differences in second-order ToM in the affective condition (Andrews et al., 2016; Wang et al., 2018). However, the previous two studies reported a significant deficit in second-order cognitive ToM, which we could not replicate in this sample using non-parametric statistics and Bonferroni corrections to account for multiple testing. It should be noted that we included a much larger sample compared to the two previous studies (64 patients with BD here, compared to 15 and 35 in previous work). Lack of power is therefore not a likely explanation for the discrepancy. Rather, it is possible that the discrepant findings may be explained by the use of different versions of the task, including differences in the number of trials for each condition. Alternatively, even though the two previous studies also included euthymic and clinically stable BD patients, it is possible that the differences between our findings could be explained by other sample characteristics, such as years of education, medication use or clinical course (e.g. history of mood episodes, hospitalizations or rapid cycling).

Overall, the findings of ToM performance equivalent to healthy controls is inconsistent with some of the broader literature showing ToM deficits in BD (although see Caletti et al., 2013; Dalkner et al., 2019; Feyerabend et al., 2018; Haag et al., 2016; Purcell et al., 2013 for exceptions). These discrepancies do not appear to be purely statistical given medium to large effect sizes in previous meta-analyses compared to the small effects seen in the current work (Bora et al., 2016; Samamé et al., 2012). Rather, they may be explained by the use of a visual task here, whereas the majority of past research has used verbal tasks. Some evidence shows that only verbal and not visual ToM may be an endophenotype for BD (Reynolds et al., 2014). Moreover, although there is evidence that social cognition in BD may be partially explained by general cognitive ability, the Yoni task was designed to have a very low memory load. In earlier work we showed moderate to large working memory (and other cognitive) deficits in several BD patients from this sample, even in the absence of ToM deficits

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here (Karantonis et al., 2020). Hence, it is unlikely that an absence of cognitive deficits can explain these negative findings. Instead, it is possible that previous ToM studies showing impairments with more cognitively taxing tasks were not entirely indexing ToM itself, but also general cognitive deficits. Finally, it is also possible that the Yoni task is not sensitive enough to elicit subtle ToM difficulties.

There were no group differences in recognition of 'fortune of others' emotions. To the best of our knowledge, the ability to infer these complex socially competitive emotional states has not previously been investigated in BD, and our findings suggest that this ability is not disproportionately affected in those with the disorder. In line with previous literature, recognition of envy and gloat correlated significantly with several ToM measures (Shamay-Tsoory, 2008; Shamay-Tsoory et al., 2007b). These findings suggest that the ability to understand socially competitive emotions is related to general ToM abilities in BD patients. Hence, the absence of group differences in the recognition of these emotions is not surprising given that ToM was not impaired in the BD group.

Previous studies in BD have reported impairments in cognitive empathy, whereas affective empathy may be spared or even increased especially during manic phases (Bodnar & Rybakowski, 2017; Cusi et al., 2010; Seidel et al., 2012; Shamay-Tsoory et al., 2009). In line with this, the BD patients in our sample reported comparable levels of affective empathy to HC's. We observed no associations between affective empathy and affective ToM or any other ToM measures, suggesting that ToM and affective empathy represent distinct concepts, consistent with previous findings that the abilities to mentalize and empathize are independent (Kanske et al., 2016; Stietz et al., 2019). An alternative explanation is that ToM was measured behaviorally, while affective empathy was examined using self-report, and these measures may not be equivalent (Dang et al., 2020; Murphy and Lilienfeld, 2019).

Finally, we did not observe any associations between ToM performance on the Yoni task and clinical variables of interest, i.e. YMRS, MADRS, estimated premorbid IQ, age of onset, age of diagnosis, number of hospitalizations, estimated lifetime manic and depressive episodes or mean lithium dose, consistent with previous findings using standard ToM tests in euthymic patients (Bora et al., 2005). However, the subsamples of patients on and off medications in our study were very small, thus caution should be taken in inferring that medications had no effect.

The present findings should be considered in the context of the strengths and limitations of the study. A key strength was that the use of the Yoni task allowed for the simultaneous assessment of both

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cognitive and affective ToM as well as first- and second-order levels of complexity. Thus, it provided a means of reducing the participant burden, and associated motivational/fatigue-related deficits, that may have arisen if using multiple different tasks to probe these subcomponents of ToM. This is also among the larger studies of ToM abilities in BD patients, giving the null findings reported here some credence. Indeed, the larger sample and minimal patient-control effect sizes compared to previous work on the topic, suggest that the negative findings observed here cannot merely be ascribed to power issues. A caveat to this is that sample may not have been powered enough to detect subtle effects if they do exist, and the results should be interpreted with this in mind.

Other limitations include the smaller number of trials in the assessment of 'fortune of others' emotions compared to the ToM conditions of the Yoni task, which is a function of the task design. Some measures, including the TEQ and some clinical variables (e.g. past mood episodes, hospitalizations) were self-reported rather than clinician rated and should therefore be interpreted with caution. General cognitive performance was also not controlled in the analyses, thus we cannot be sure that the findings are independent of level of cognitive functioning. Nonetheless, we included the WTAR as an estimate of premorbid IQ, and despite group differences between BD patients and healthy controls, scores were not associated with the Yoni data. Finally, the use of a cross-sectional design did not allow us to examine how time-varying symptoms of BD influence ToM and recognition of 'fortune of others' emotions. To more thoroughly understand state and trait effects, a longitudinal study is needed to investigate if changes in performance on the Yoni task occur with changes in symptom levels in the same individuals. In our study, we observed similar findings when the sample was restricted to euthymic BD patients only, and none of the ToM measures correlated with mood symptoms. Thus, our findings do suggest that ToM and recognition of 'fortune of others' emotions in BD patients do not vary according to mood state. However, given the presence of null findings in this study in the context of previous research showing ToM deficits in euthymic BD patients, longitudinal work would help to clarify the nature of social cognitive functioning in BD even further.

Irrespective of these limitations, the current findings enhance our understanding of the social cognitive profile in BD by highlighting ToM and empathy as areas of potentially spared functioning. Given evidence that many patients with BD have experienced adversity during developmental periods in which these abilities develop, our findings suggest that intact ToM and empathy may be markers of resilience in BD (Etain et al., 2008; Watson et al., 2014). Knowledge that ToM and empathy is intact is

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particularly relevant in light of an increased focus on the importance of considering cognitive strengths in the context of approaches to remediate cognitive deficits (Allott et al., 2020). This could be done by considering practical ways that a patients' knowledge of intact ToM and empathy could be utilized to reduce self-stigma and promote self-efficacy, improved well-being and functioning (Allott et al., 2020). Hence these findings are important for therapeutic interventions to support functional recovery in BD. In sum, we observed intact cognitive and affective ToM in BD patients using a visual task, no deficit in recognition of 'fortune of others' emotions, and levels of affective empathy comparable to HC's. There appears to be some overlap between ToM and recognition of 'fortune of others' emotions, whereas ToM and affective empathy seem to be unrelated. However, future studies should examine empathy behaviorally and include measures of cognitive empathy.

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Table 1: Demographic and clinical variables for bipolar disorder (BD) patients and healthy controls (HC)

	HC (N=34)	BD (N=64)	Statistical test
Age, Mean (SD)[1]	35.82 (11.85)	37.11 (11.21)	T(1, 95) = 053, p = .598
Sex, N (%)			
Male	15 (44%)	33 (52%)	Chi^2 (1) = 0.49, p = .483
Female	19 (56%)	31 (48%)	
Estimated premorbid IQ (WTAR), Mean (SD)[2]	114.91 (8.65)	107.69 (11.52)	U = 557.0, p <.001
Medication, N (%)			
Mood stabilizer	-	39 (61%)	
Antidepressants		20 (31%)	
Typical antipsychotics		2 (3%)	
Atypical antipsychotics		30 (47%)	
Age of onset, Mean (SD)[3]	-	22.48 (9.42)	
Age at diagnosis, Mean (SD)[4]	-	28.56 (10.04)	
Number of hospitalizations due to mood disturbances, Mean (SD)[5]	-	3.60 (4.99)	
Number of manic episodes (estimated lifetime), Mean (SD)[6]	-	17.62 (30.97)	
Number of depressive episodes (estimated lifetime), Mean (SD)[7]	-	25.78 (38.46)	
Bipolar type, N (%)			
Type I	-	60 (94%)	
Type II		4 (6%)	
YMRS total, Mean (SD)	-	3.39 (2.96)	
MADRS total, Mean (SD)	-	7.87 (7.20)	

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History of psychosis[8]			
Yes	-	38 (60%)	
No	-	25 (40%)	

Note: T = Independent samples t-test. U = Mann Whitney U test. WTAR: Wechsler Test of Adult Reading task, YMRS: Young Mania Rating Scale, MADRS: Montgomery Asberg Depression Rating Scale. [1]Missing data from 1 bipolar disorder (BD) patient. [2]Missing data from 3 BD patients.[3]Missing data from 8 BD patients. [4]Missing data from 5 BD patients. [5]Missing data from 4 BD patients. [6]Missing data from 3 BD patients. [7]Missing data from 4 BD patients. [8]Missind data from 1 patient.

Table 2: Average Yoni performance for bipolar disorder (BD) patients and healthy controls (HC).

	HC (N=34)	BD (N=64)	Statistical test
First-order accuracy			
Cognitive	95.10 (13.32)	97.14 (10.09)	U = 938.5 p = .112
Affective	97.30 (9.56)	97.14 (8.81)	U = 1048.5, p = .628
Physical	94.85 (14.14)	91.41 (17.94)	U = 965.5, p = .210
First-order RT			
Cognitive	4226.28 (1566.72)	3438.50 (1056.26)	U = 702.0, p = .004
Affective	3667.00 (1492.20)	3293.13 (1019.07)	U = 912.0, p = .189
Physical	2528.29 (728.84)	2923.41 (1121.83)	U = 894.0, p = .148
Second-order accuracy			
Cognitive	83.33 (14.94)	75.78 (18.76)	U = 837.5, p = .058
Affective	86.52 (11.96)	79.69 (17.81)	U = 889.5, p = .131
Physical	90.20 (14.86)	88.28 (16.71)	U = 1034.0, p = .651

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Second-order RT			
Cognitive	8286.55 (2863.65)	8625.06 (2668.28)	U = 1012.0, p = .571
Affective	6747.12 (1890.53)	7174.52 (2201.28)	U = 1005.0, p = .536
Physical	4796.10 (1664.39)	5317.37 (2202.29)	U = 997.0, p = .497
Fortune-of-others			
accuracy	82.35 (16.38)	80.21 (23.55)	U = 1059.5, p = .823
Gloat	88.24 (16.68)	76.56 (32.22)	U = 901.5, p = .134
Envy	88.73 (16.78)	90.63 (12.20)	U = 1050.0, p = .750
Identifies	87.25 (17.91)	85.68 (20.55)	U = 1065.0, p = .847
Physical #2			
Fortune-of-others RT			
Gloat	6655.23 (2935.84)	6067.81(1901.87)	U = 1001.0 p = .516
Envy	6237.19 (3051.40)	6377.92 (2617.35)	U = 1040.0, p = .720
Identifies	5294.61 (2180.84)	5051.08 (1985.81)	U = 977.0, p = .407
Physical #2	5349.72 (2239.58)	5671.00 (2264.68)	U = 1001.0, p = .516
TEQ total score[1]	49.61 (7.60)	48.13 (7.70)	T (1, 92) = -0.883, p = .379

Note: Values are given as mean (SD). U = Mann Whitney U test. T = Independent samples t-test. No significant group differences were observed using a Bonferroni-adjusted alpha level of $p < .002$ (.05/21) to account for multiple comparisons. The euthymic patients are included in the full bipolar disorder (BD) group. Accuracy is given in percent correct and response time (RT) is given in milliseconds. [1] Missing data from 1 BD patients and 3 HC´s.

Table 3: Inter-correlations between ToM, 'fortune of others' emotions and affective empathy in the full sample

A: Inter-correlations between accuracy variables from the Yoni task and TEQ total score

	Envy	Gloat	Identification	Physical #2	TEQ total
First-order cognitive	.174	.132	.143	-.048	.052
First-order affective	**.346**	.171	.161	.159	.126

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First-order physical	.236	.131	-.021	.811	.124
Second-order cognitive	**.372**	.325	.133	.256	-.074
Second-order affective	**.463**	**.359**	.077	.235	-.062
Second-order physical	.332	.261	-.054	.251	-.077
TEQ total	-.062	-.054	.008	.086	-

B: Inter-correlations between reaction time variables from the Yoni task and the TEQ total score

	Envy	Gloat	Identification	Physical #2	TEQ total
First-order cognitive	**.371**	**.451**	**.536**	.307	-.313
First-order affective	**.411**	**.543**	**.571**	**.480**	-.193
First-order physical	.302	**.346**	.333	.262	-.161
Second-order cognitive	**.595**	**.545**	**.658**	**.638**	-.265
Second-order affective	**.439**	**.483**	**.468**	**.494**	-.224
Second-order physical	**.426**	**.456**	**.453**	**.473**	-.082
TEQ total	**-.369**	-.201	-.335	-.158	-

Note: Values represent spearman's correlations. Correlations significant at a Bonferroni-adjusted alpha level of $p < .0007$ (.05/68) are displayed in bold.

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