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Review article

Social cognition throughout the three phases of bipolar disorder: A state-of-the-art overview

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ABSTRACT

Although it is now well documented that bipolar disorder (BD) often presents with cognitive deficits and suboptimal social adjustment, the social cognitive profile of the illness throughout its three phases remains unclear. An extensive search was conducted through the online databases EBSCO, PsychInfo, PubMed, ScienceDirect, and Wiley–Blackwell, covering the period between 1990 and 2012. Fifty-one studies comparing the social cognitive performance of bipolar patients with that of healthy controls were identified. Deficits in emotion recognition and theory of mind were found in manic, depressed, and euthymic bipolar subjects. Furthermore, altered face emotion recognition and brain-related abnormalities were noted both in euthymic patients and subjects at risk for BD. The influence of clinical and neurocognitive variables on the social cognitive performance of bipolar patients remains to be ascertained. Future directions for research are discussed.

Contents

1. Introduction

To date, a large body of work has attempted to define the neuropsychological profile of subjects affected by bipolar disorder (BD) throughout the three phases of the illness. As shown by numerous studies, BD patients display conspicuous cognitive dysfunctions in a variety of domains, even during periods of clinical remission (Torres et al., 2007; Bora et al., 2011; Mann-Wrobel et al., 2011). Such impairments correlate negatively with social and occupational adjustment (Martínez-Arán et al., 2004; Martino et al., 2008; Harvey et al., 2010) and have been consistently recognized as strong predictors of long-term functional outcome (Tabarés-Seisdedos et al., 2008; Martino et al., 2009; Bonnín et al., 2010). Although mood symptoms and deleterious effects of pharmacological treatment may account partly for defective neuropsychological performance, the fact that first-degree unaffected relatives of BD patients exhibit a similar pattern

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of impairment (Arts et al., 2008; Bora et al., 2009) suggests that cognitive dysfunction may be a core feature of the pathophysiology of the illness and an expression of its strong genetic component.

Despite the rapid growth in scientific research on cognitive aspects of mood disorders over the past years, there is a large knowledge gap concerning social cognition in BD. Social cognition is generally defined as a complex set of high order neuropsychological processes that subserve adaptive social behavior (Adolphs, 1999; Amodio and Frith, 2006). With the aim of providing an organizing framework, the National Institute of Mental Health has delimited five dimensions within social cognition, namely theory of mind, social perception, social knowledge, attributional bias, and emotion processing (Green et al., 2008). However, this categorization is not yet conclusive, since there is some overlap among such social cognitive areas. Furthermore, social cognition may encompass a larger set of components that have not been adequately addressed in research studies on clinical samples conducted so far. Indeed, most investigations of BD have only focused on theory of mind and emotion processing. Theory of mind – ToM – also known as mentalizing or mindreading, is a key aspect of social cognition that refers to the ability to attribute mental states such as beliefs, intents and desires, to oneself and others (Premack and Woodruff, 1978). This capability encompasses distinct components, including the understanding of other people's thoughts, recognition of lie and irony, and gaze monitoring, which appear at different developmental stages. Mentalizing abilities entail both cognitive and affective aspects (Shamay-Tsoory and Aharon-Peretz, 2007; Kalbe et al., 2010; Shamay-Tsoory, 2011). Cognitive ToM is the ability to make inferences about other people's beliefs, whereas affective ToM refers to the capability to infer others' emotions. Closely related to the latter, *emotion processing* comprises a set of different processes that enable an individual to perceive and utilize emotions (Green et al., 2008). A salient aspect of this construct involves the ability to recognize and appraise the so called 'basic' emotions expressed by others through visual and verbal cues. Basic emotions such as fear, sadness, disgust, happiness, anger, and surprise, are thought to be innate, automatic, and to have universally recognizable facial expressions (Darwin, 1872; Ekman and Friesen, 1976).

Given the compelling evidence for poor social functioning in about two-thirds of bipolar subjects (Goldberg and Harrow, 2004; Huxley and Baldessarini, 2007; Wingo et al., 2010), the question regarding the presence of social cognitive deficits in BD – and whether they are state or trait dependent – has arisen in the last decade, promoting research on emotion processing and theory of mind across the three phases of the illness. Nevertheless, studies have failed to provide consistent results, which not only may be due to the heterogeneous presentation of the disorder, but also to several methodological shortcomings. Therefore, the nature of social cognitive functioning in BD remains to be ascertained.

The main aims of this article were to present an overview of the current evidence on two social cognitive domains, namely theory of mind and emotion processing, in bipolar patients across the three phases of the illness and to identify targets for future neuropsychological research.

2. Materials and methods

2.1. Search strategy

The online databases EBSCO, PsychInfo, PubMed, ScienceDirect, and Wiley–Blackwell were searched using combinations of the following keywords: *bipolar disorder, mania, cognitive functioning, neuropsychology, social cognition, mindreading, theory of mind, mentalizing, emotion perception, emotion recognition,* and *emotion processing*. The reference lists of review articles on cognitive functioning in BD and the studies identified for inclusion were also searched for further relevant reports.

2.2. Selection criteria

Articles were considered for the current review if they met the following criteria: (i) were published in English between January 1990 and November 2012. (ii) Reported behavioral results for social cognitive domains (facial emotion recognition or theory of mind) in BD patients. (iii) Used standardized diagnostic criteria to ascertain diagnosis. (iv) Included a healthy comparison group or normative data for standardized tests. (v) Provided information about patients' mood state. (vi) Studies including patients with different psychiatric diagnoses provided separate data for BDs' social cognitive performance. (vii) Studies including BD patients in different phases of the illness (manic, depressed, euthymic) provided separate data for each bipolar subgroup.

After conducting a revision of studies exploring social cognition in BD patients, investigations were classified into two categories according to the tasks employed: *theory of mind* and *emotion recognition*. The results for each social-cognitive aspect were then reported.

3. Results

Fifty-one studies meeting the seven selection criteria were identified and thus considered for the present systematic review. Fifteen studies explored ToM (Table 1) and 41 reports examined emotion processing (Table 2) in bipolar patients.

3.1. Theory of mind

Different types of instruments, with varying levels of complexity, have been used to assess the ability to attribute mental states in BD patients. The most basic mentalizing measures are False Belief recognition tasks (Corcoran et al., 1995; Fletcher et al., 1995; Frith and Corcoran, 1996), which assess an aspect of ToM that first manifests itself around 3–4 years of age, when children are capable of understanding that others may hold beliefs that are different from reality (first order false belief). A more complicated version of the task taps into the ability to infer the false belief of one character about the belief of a second character (second order false belief).

Other ToM tasks used in investigations of BD patients assess developmentally more advanced skills, which not only require subjects to understand the difference between the speaker's beliefs and those of the listener, but also to empathically appreciate the listener's emotional state (Kalbe et al., 2010). Among these tasks, the *Faux Pas* recognition test (Stone et al., 1998), assesses the capability to understand that there are certain things that the others may not want to hear and thus should not be said. The Hinting Task (Corcoran et al., 1995) and Happé's Strange Stories Task (Happe, 1994) require subjects to distinguish between literal and intended meaning. 'Eyes tasks' based on Baron-Cohen et al. (2001) assess the ability to appraise others' mental states by watching the ocular region of faces. It has been suggested that, unlike verbal ToM tasks, Eyes tests depend mainly on automatic decoding abilities rather than reasoning about mental states (Tager-Flusberg and Sullivan, 2000; Sabbagh, 2004). The 'Movie for the Assessment of Social Cognition' – MASC – (Dziobek et al., 2006) is another advanced task that has been used for the assessment of bipolar patients. This test includes more realistic stimuli integrating voice, gestures, and contextual information and taps into the capacity to attribute different modalities of mental states such as thoughts, feelings, and intentions. Finally, a less commonly used task with a higher level of abstraction is the Theory of Mind Animation Task (Abell et al., 2000), which requires subjects to attribute complex mental states to geometric shapes mimicking human social behavior.

Studies exploring adult BD subjects' performance on ToM tasks have all consistently reported mentalizing impairment of large

Table 1
Main studies exploring bipolar patients' performance on ToM tasks. Cut-off scores on mood rating scales used to ascertain euthymia/subsyndromal state are given.

Primary study	Sample	Mean age	Definition of euthymia	Task	Results
Euthymia/subsyndromal state					
Barrera et al. (2012)	12 BD I–II, 12 HC euthymic $n=12$	48.2	HDRS < 7, YMRS < 8	Faux pas recognition, Eyes test	Preserved performance on the Eyes Test. BDs performed below the cut-off score on the Faux Pas test. However, no significant patient-control differences were observed
Bora et al. (2005)	43 BD I, 30 HC euthymic $n=43$	38.6	HDRS < 7, YMRS < 6	Hinting task, Eyes test	Impaired
Ibanez et al. (2012)	13 BD II, 13 HC euthymic $n=13$	40.1	MADRS ≤ 8, YMRS < 6	Faux pas recognition, Eyes test	Preserved performance on the Eyes Test. Impaired Faux Pas recognition
Inoue et al. (2004)	16 BD (type?), 34 MDD, 50 HC euthymic $n=16$	44.5	Remitted depression: HDRS ≤ 7	1st And 2nd order false belief	Impaired
Kerr et al., 2003	48 BD (type?), 15 HC euthymic $n=13$	46.8	BDI, BMS. Cut off scores?	1st And 2nd order false belief	Preserved
Lahera et al. (2008)	75 BD I, 48 HC euthymic $n=75$	48.2	HDRS < 8, YMRS < 8	Happé's Strange Stories	Impaired
Lahera et al. (2012)	39 BD I–II, (n?) HC euthymic $n=39$	46.8	HDRS < 8, YMRS < 6	Faux pas recognition	Low-functioning BDs showed a significant impairment compared with high-functioning BDs. Globally, BDs did not show significant impairments compared with HCs
Malhi et al. (2008)	20 BD I, 20 HC euthymic $n=20$	35.3	HDRS ≤ 6, YMRS ≤ 6	Complex ToM task including abstract stimuli	Impaired task performance. Different pattern of brain activation: less cortical involvement was observed in BDs
Martino et al. (2011)	81 BD I–II, 34 HC euthymic $n=81$	39.8	HDRS ≤ 8, YMRS ≤ 6	Faux pas recognition, Eyes test	Impaired faux pas recognition.
McKinnon et al. (2010)	14 BD I–II-NOS, 14 HC subsyndromal state $n=14$	47.5	Subsyndromal state: 7 ≤ HDRS ≤ 15; YMRS < 10	1st And 2nd order false belief	Impaired
Montag et al. (2010)	29 BD I, 29 HC euthymic $n=29$	44	HDRS < 14, YMRS < 5	MASC	Selective deficit of cognitive aspects of ToM
Olley et al. (2005)	15 BD I, 13 HC euthymic $n=15$	39.2	HDRS < 12, YMRS < 12	2nd order ToM	Impaired performance (only on verbal, but not visual, tasks)
Shamay-Tsoory et al. (2009)	19 BD I, 20 HC euthymic $n=19$	40.2	HDRS ≤ 9, YMRS ≤ 7	Faux pas recognition, Eyes test	Impaired cognitive but not affective faux pas. Complex emotions recognition was preserved
Wolf et al. (2010)	33 BD I, 29 HC euthymic $n=11$	49.7	HDRS < 15, YMRS < 12	1st, 2nd, And 3rd order ToM	Impaired
Mania					
Kerr et al. (2003)	48 BD (type?), 15 HC manic $n=20$	41.3		1st And 2nd order false belief	Impaired
Sarfati and Hardy-Bayle (1999)	10 BD I, 25 SCH, 15 HC manic $n=10$	33.9		Theory of Mind Comic Strip	BDs performed significantly worse than HCs, but better than disorganized SCHs
Wolf et al. (2010)	33 BD I, 29 HC manic $n=10$	45.4		1st, 2nd, And 3rd order ToM	Impaired
Depression					
Kerr et al. (2003)	48 BD (type?), 15 HC depressed $n=15$	45.1		1st And 2nd order false belief	Impaired
Wolf et al. (2010)	33 BD I, 29 HC depressed $n=12$	47.8		1st, 2nd, And 3rd order ToM	Impaired

BD: bipolar disorder subjects; HC: healthy controls; MDD: major depressive disorder subjects; SCH: schizophrenia subjects; NOS: bipolar disorder not otherwise specified; YMRS: Young Mania Rating Scale; HDRS: Hamilton Depression Rating Scale; BDI: Beck Depression Inventory; MASC: Movie for the Assessment of Social Cognition; ToM: theory of mind; ?: not given.

effect size in both manic (Sarfati and Hardy-Bayle, 1999; Kerr et al., 2003; Wolf et al., 2010) and depressed adult patients (Kerr et al., 2003; Wolf et al., 2010). Findings were also consistent during euthymia: eleven out of thirteen reports communicated positive results in at least one mentalizing aspect (Inoue et al., 2004; Bora et al., 2005; Olley et al., 2005; Lahera et al., 2008; Malhi et al., 2008; Shamay-Tsoory et al., 2009; Montag et al., 2010; Wolf et al., 2010; Martino et al., 2011; Barrera et al., 2012; Ibanez et al., 2012) with effect sizes in the moderate and large range for most measures of ToM, with the exception of Eyes tasks. A study including patients in subsyndromal state also reported mindreading dysfunctions of large magnitude for false belief and faux pas recognition (McKinnon et al., 2010). Only two studies (Kerr et al., 2003; Lahera et al., 2012) did not find any patient-control differences for mentalizing skills (first and second order false belief and faux pas recognition respectively). Performance was preserved on mentalizing tasks requiring the inference of mental states through the eye region of faces. At present, five investigations examined the ability to 'read the mind in the eyes', yielding both negative (Shamay-Tsoory et al., 2009; Martino et al., 2011; Barrera et al., 2012; Ibanez et al., 2012) and positive results with small patient-control effect sizes (Bora et al., 2005).

Table 2
Main studies exploring bipolar patients' performance on emotion processing tasks. Cut-off scores on mood rating scales used to ascertain euthymia/subsyndromal state are given.

Primary study	Sample	Mean age	Definition of euthymia	Task	Results
Euthymia/subsyndromal state/stability					
Addington and Addington (1998)	40 BD (type?), 40 SCH, 40 HC stable $n=40$	38.5	Stability	Matching Labeling	BDs performed significantly more poorly than HCs on a matching task, but not as poorly as SCHs. BDs' labeling performance was preserved
Almeida et al. (2010)	30 BD I, 15 MDD, 15 HC euthymic $n=15$	34.9	HDRS. Cut off score?	Labeling	BDs were less accurate than HCs at recognizing happiness
Bora et al. (2005)	43 BD I, 30 HC euthymic $n=43$	38.6	HDRS <7, YMRS <6	Labeling	Preserved
Bozikas et al. (2006)	19 BD I, 30 HC euthymic $n=19$	39	MADRS ≤ 8, YMRS ≤ 8	Matching	Impairment in BD patients was restricted to the matching of facial emotional expressions despite their intact perception of facial identity.
Derntl et al. (2009)	62 BD I–II, 62 HC subsyndromal state $n=62$	43	Subsyndromal state: MADRS ≤ 18 YMRS ≤ 13	Labeling	Impaired (only in BD I)
Foland-Ross et al. (2012)	24 BD I, 26 HC euthymic $n=24$	38.8	HDRS ≤ 7, YMRS ≤ 7	Labeling Matching	Preserved labeling/matching of fear and anger. Neuroimaging results showed that BDs exhibited a significant decrease in activation of the right vlPFC
Harmer et al. (2002)	20 BD (type?), 20 HC euthymic $n=20$	37.8	HDRS ≤ 8, YMRS ≤ 8	Labeling	Preserved overall accuracy. Facilitated recognition of disgust
Hassel et al. (2008)	19 BD I, 24 HC euthymic $n=19$	32.5	HDRS <11, YMRS <10	Labeling	Preserved task performance. Abnormal patterns of subcortical limbic and dorsal prefrontal cortical activity in response to emotional faces were observed in BDs
Hassel et al. (2009)	14 BD I, 16 HC euthymic $n=14$	32.6	HDRS <14, YMRS <10	Labeling	Differences between BDs and HCs were not significant. BDs showed reduced dorsal prefrontal-cortical activity to all faces. Only BDs showed greater subcortical-striatal activity to happy and neutral faces
Hoertnagl et al. (2011)	47 BD I, 45 HC euthymic $n=47$	42.2	MADRS ≤ 8, YMRS ≤ 8	Labeling	Patients were particularly impaired in the recognition of facial expressions depicting disgust and happiness
Hulvershorn et al. (2012)	75 BD I–II, 30 HC euthymic $n=15$	33.8	HDRS <10, YMRS <10	Matching	Preserved overall accuracy. Abnormalities in corticolimbic activation were seen in response to negative facial emotion processing in BDs.
Ibanez et al. (2012)	13 BD II, 13 HC euthymic $n=13$	40.1	MADRS ≤ 8, YMRS <6	Valence rating	Preserved accuracy. BDs displayed abnormal cortical processing of emotional faces
Jogia et al. (2008)	12 BD I, 12 HC stable $n=12$	42.1	HDRS <14, YMRS <7	Labeling	Preserved recognition of sad facial affect. BDs showed overactivity in temporal regions and underactivity in the dorsal medial and right ventrolateral prefrontal cortex, and the dorsal cingulate gyrus
Kim et al. (2009)	14 BD I, 14 HC euthymic $n=14$	30.4	HDRS ≤ 7,YMRS ≤ 5	Labeling	Preserved overall accuracy in the recognition of happy, angry and neutral facial expressions. Delayed reaction times in emotional conditions compared with HC. Reduced activations in the 'mirror neuron system'
Lahera et al. (2012)	39 BD I–II, (n?) HC euthymic $n=39$	46.8	HDRS <8, YMRS <6	Labeling	Low-functioning BDs showed a significant impairment compared with high-functioning BDs. Globally, both bipolar groups showed a significant impairment in facial emotion recognition compared with a similar sample of HCs
Lembke and Ketter (2002)	24 BD I–II, 10 HC euthymic $n=16$	?	HDRS <10, YMRS <10	Labeling	Enhanced fear recognition in euthymia (only in BD II)
Lagopoulos and Malhi (2011)	11 BD I, 11 HC euthymic $n=11$	33.3	HDRS ≤ 6, YMRS ≤ 6	Labeling	Both BDs and HCs were able to similarly distinguish between neutral and disgust face expression stimuli. Unlike HCs, BDs did not exhibit any frontal activation
Malhi et al. (2007)	10 BD I, 10 HC euthymic $n=10$	33.5	HDRS ≤ 6, YMRS ≤ 6	Labeling	BDs were equally accurate at identifying facial expressions as HCs, but were slower to respond to fear and disgust. BD patients showed increased response to fear, while HCs responded more to disgust (with differential hippocampus and amygdala activation)
Martino et al. (2008)	50 BD I–II, 30 HC euthymic $n=50$	42	HDRS $\leq$ 8, YMRS ≤ 6	Labeling	Impaired recognition of disgust and fear
Martino et al, (2011)	81 BD I–II, 34 HC euthymic $n=81$	39.8	HDRS ≤ 8, YMRS ≤ 6	Labeling	Impaired recognition of fear
McClure et al. (2003)	11 BD (type?), 10 AD, 25 HC euthymic $n=11$	13.7	?	Labeling	BD youths performed worse than anxious adolescents and HCs
McClure et al. (2005)	40 BD I–II, 22 HC euthymic $n=40$	12.9	CDRS ≤ 40, YMRS ≤ 11	Labeling	Impaired
Pavuluri et al. (2007)	10 BD I, 10 HC euthymic $n=10$	14.9	CDRS, YMRS Cut off scores?	Labeling	Response accuracy (recognition of happiness and anger) and latency were similar in BD and HC groups. BDs exhibited abnormal activation of right rostral ventrolateral prefrontal cortex, right pregenual anterior cingulate, amygdala, and paralimbic cortex
Pavuluri et al. (2009)	10 BD I, 10 HC euthymic $n=10$	16.2	CDRS, YMRS Cut off scores?	Labeling	Response accuracy (recognition of happiness and anger) and latency were similar in BD and HC groups, though differential brain activation was observed
Robinson et al. (2008)	15 BD I, 16 HC euthymic $n=15$	38.5	HDRS, YMRS cut off scores?	Matching	Preserved task performance. BD patients showed hyperactivation in inferior prefrontal cortical regions compared with controls
Shamay-Tsoory et al. (2009)	19 BD I, 20 HC euthymic $n=39$	40.2	HDRS ≤ 9, YMRS ≤ 7	Labeling	Preserved

Table 2 (*continued*)

Primary study	Sample	Mean age	Definition of euthymia	Task	Results
Schenkel et al. (2007)	58 BD I, 28 HC euthymic $n=29$	11.9	CDRS < 40, YMRS ≤ 8	Identification Discrimination Intensity	BD subjects showed marked impairments in the ability to correctly identify emotionally intense happy and sad facial expressions, and tended to misjudge extreme facial expressions as being moderate to mild in intensity
Soeiro-de-Souza et al. (2012b)	39 BD I, 40 HC euthymic $n=39$	32.9	HDRS, YMRS cut off scores?	Labeling	BDs displayed impaired performance. The CACNA1C risk allele for BD was associated with emotion recognition impairment in BD, while in controls nothing was observed
Surguladze et al. (2010)	20 BD I, 20 FDR, 20 HC euthymic $n=20$	42.7	?	Intensity	Preserved task performance. Exaggerated medial prefrontal cortical and subcortical (putamen and amygdala) responses to emotional signals were observed in patients and in their FDR
Vaskinn et al. (2007)	21 BD I, 31 SCH, 21 HC euthymic $n=21$	38.1	IDS-C < 30, YMRS < 12	Identification Discrimination	Preserved
Venn et al. (2004)	17 BD I–II, 17 HC euthymic $n=17$	44.4	HDRS < 8, YMRS < 8	Labeling	Preserved
Yurgelun-Todd et al. (2000)	14 BD (type?), 10 HC stable $n=14$	31.6	Clinical stability	Labeling	Impaired ability to identify fear expression. BDs exhibited a reduction in dorsolateral prefrontal cortex activation and an increase in amygdalar activation in response to fearful facial affect
Mania					
Bermpohl et al. (2009)	10 BD I, 10 HC manic $n=10$	37.9		Labeling	BDs showed higher valence ratings in positive pictures and associated enhanced amygdala activation. Positive correlation between amygdala activation and YMRS scores
Chen et al. (2006)	16 BD I, 8 HC manic $n=8$	39		Labeling	No between group diffferences in task performance were observed, though manic patients tended to underestimate intensity of sad facial expressions
Foland et al. (2008)	9 BD I, 9 HC manic $n=9$	34.6		Matching Labeling	Preserved task performance. Compared with HC, BD patients had a significantly reduced VLPFC regulation of amygdala response during the emotion labeling task
Getz et al. (2003)	25 BD (type?), 25 HC manic/mixed $n=25$	25.3		Matching Labeling	BD patients were selectively impaired on a facial affect labeling task
Gray et al. (2006)	23 BD I–II, 21 HC manic $n=9$	46.8		Labeling	Preserved
Hulvershorn et al. (2012)	75 BD I–II, 30 HC manic $n=30$	33.8		Matching	Preserved overall accuracy. Abnormalities in corticolimbic activation were seen in response to negative facial emotion processing in BDs
Lennox et al. (2004)	10 BD I, 12 HC manic $n=10$	37.3		Intensity	Attenuated subjective rating of the intensity of sad facial affect, associated with diminished activation in the subgenual anterior cingulate and bilateral amygdale and increased activation in the posterior cingulate and posterior insula
Lembke and Ketter (2002)	24 BD I–II, 10 HC manic $n=8$	?		Labeling	Impaired (only in mania). Enhanced fear recognition in euthymia (only in BD-II)
Schenkel et al. (2007)	58 BD I, 28 HC manic/mixed $n=29$	11.9		Identification Discrimination Intensity	BD subjects showed marked impairments in the ability to correctly identify emotionally intense happy and sad facial expressions, and tended to misjudge extreme facial expressions as being moderate to mild in intensity
Soeiro-de-Souza et al. (2012a)	64 BD I, 75 HC manic $n=39$	28.2		Labeling	BDs displayed impaired performance. Bipolar manic patients carrying the COMT Met allele recognized fewer surprised faces
Depression					
Almeida et al. (2010)	30 BD I, 15 MDD, 15 HC depressed $n=15$	34.9		Labeling	BDs were less accurate than HCs when labeling the emotion of faces during the happy emotion experiment. BD patients showed elevated left amygdala activity to mild and neutral facial expressions in the sad emotion experiments
Chen et al. (2006)	16 BD I, 8 HC depressed $n=8$	39		Labeling	No between group diffferences in task performance were observed
Gray et al. (2006)	23 BD I–II, 21 HC depressed $n=14$	46.8		Labeling	Preserved. Depressed patients showed impaired sensitivity to happiness and enhanced sensitivity to other emotions
Hulvershorn et al. (2012)	75 BD I–II, 30 HC depressed $n=30$	33.8		Matching	Preserved overall accuracy. Abnormalities in corticolimbic activation were seen in response to negative facial emotion processing in BDs
Schaefer et al. (2010)	21 BD I, 34 MDD, 24 HC depressed $n=21$	46.8		Labeling	BD patients appeared to require more intense stimuli before they could correctly identify affect expressions, but tended to be relatively accurate when labeling emotions
Soeiro-de-Souza et al. (2012a)	64 BD I, 75 HC depressed $n=25$	28.2		Labeling	BDs displayed impaired performance
Summers et al. (2006)	36 BD I–II compared with normative data. depressed $n=36$	39		Labeling	Impaired, with deficits being more severe in BD II

BD: bipolar disorder; HC: healthy controls; MDD: major depressive disorder; AD:anxiety disorders; SCH: schizophrenia; YMRS: Young Mania Rating Scale; HDRS: Hamilton Depression Rating Scale; CDRS: Children Depression Rating Scale; MADRS: Montgomery-Asberg Depression Rating Scale; FDR: first degree relatives of patients with BD; ?: not given.

Finally, only two studies looked at the relationship between cognitive and affective aspects of ToM (Shamay-Tsoory et al., 2009; Montag et al., 2010). Both investigations reported altered cognitive, but intact affective ToM in euthymic subjects assessed with the Faux pas task and the Movie for the Assessment of Social Cognition.

3.2. Emotion processing

Most investigations assessing emotion recognition in BD required subjects to either match (matching paradigms) or name (labeling paradigms) pictures of facial expressions according to the emotion displayed. The most commonly utilized tasks in research on bipolar disorders included the stimuli created by Ekman and Friesen (1976), which consist of posed facial expressions of basic emotions. A pioneering study into emotion processing in euthymic bipolar patients (Addington and Addington, 1998) aimed to compare schizophrenics with remitted BD subjects and revealed the presence of less pronounced dysfunctions in the latter. However, bipolar patients exhibited significant differences of large magnitude for the performance on a matching emotion processing paradigm compared to healthy controls. Similarly, large deficits in the matching of six basic emotions were found by Bozikas et al. (2006) in a sample of remitted patients. Contrarily, assessing the processing of a smaller number of emotions, Hulvershorn et al. (2012) and Foland-Ross et al. (2012) did not find any differences for the matching of negative emotions (anger/fear).

In euthymic subjects, emotion labeling paradigms assessing the recognition of at least six basic emotions were utilized in twelve studies, out of which nine documented no significant patient-control differences regarding total accuracy (Addington and Addington, 1998; Harmer et al., 2002; Lembke and Ketter, 2002; Venn et al., 2004; Bora et al., 2005; Vaskinn et al., 2007; Martino et al., 2008, 2011; Shamay-Tsoory et al., 2009), and three (Hoertnagl et al., 2011; Lahera et al., 2012; Soeiro-de-Souza et al., 2012b) reported positive results. However, only six of these studies assessed each of the emotions separately. For instance, Martino et al. (2008, 2011) found diminished recognition of fear in the presence of spared overall accuracy in remitted patients. Similarly, Venn et al. (2004) found a trend towards significance for fear recognition, whereas Harmer et al. (2002) reported that recognition of disgust was facilitated in BD patients. Hoertnagl et al. (2011) found diminished recognition of disgust and happiness, and Lembke and Ketter (2002) reported that the performance of euthymic subjects with BD I or BD II was similar to that of healthy comparison subjects across all emotions. Other studies assessing a smaller number of affect expressions in remitted patients found delayed response times for the recognition of fear and disgust (Malhi et al., 2007), happiness and anger (Kim et al., 2009) and impaired recognition of fear (Yurgelun-Todd et al., 2000) and happiness (Almeida et al., 2010).

Finally, abnormal brain functioning, mainly reduced prefrontal activation, has consistently been noted in euthymic/stable subjects during the performance on both matching and labeling paradigms (Yurgelun-Todd et al., 2000; Malhi et al., 2007; Hassel et al., 2008; Jogia et al., 2008; Kim et al., 2009; Lagopoulos and Malhi, 2011; Foland-Ross et al., 2012).

On the other hand, three out of four studies assessing emotion labeling in adult manic patients reported impaired performance (Lembke and Ketter, 2002; Getz et al., 2003; Soeiro-de-Souza, 2012a). Besides, a selective deficit in the recognition of fear and disgust (Lembke and Ketter, 2002) was reported. Similarly, Gray et al. (2006) in the presence of a preserved overall performance, reported a tendency to perceive fear less accurately. Moreover, three out of four investigations assessing intensity rating of emotions have consistently reported a trend towards misjudging sad expressions during mania (Lennox et al., 2004; Chen et al., 2006; Bermpohl et al., 2009). Similarly, during depression both positive (Almeida et al., 2010; Surguladze et al., 2010; Soeiro-de-Souza et al., 2012a) and negative (Gray et al., 2006; Schaefer et al., 2010) results have been observed as well as mood congruent bias (differential reduction in sensitivity to facial happiness) (Gray et al., 2006).

Investigations conducted with euthymic pediatric BD patients reported both negative (Pavuluri et al., 2007, 2009) and positive results (McClure et al., 2003, 2005; Schenkel et al., 2008). Positive results have also been noted in manic unmedicated patients (Schenkel et al., 2007). Finally, some investigations (Pavuluri et al., 2007, 2009) by means of functional magnetic resonance imaging demonstrated abnormal activation of right rostral ventrolateral prefrontal cortex, right pregenual anterior cingulate, amygdala, and paralimbic cortex during task performance.

3.3. The relationship between social cognition and clinical variables

At present, very few studies have studied the relation between social cognition and clinical variables. A major shortcoming in neuropsychological research regards the neglect of heterogeneity within BD, since most studies have examined BD as a homogeneous category or else focused exclusively on BD I. Only six studies have compared the social cognitive performance of BD I with that of BD II. Recent investigations found no significant differences among both bipolar subgroups with respect to affect recognition (Martino et al., 2008, 2011) and theory of mind (Martino et al., 2011). Contrarily, Lembke and Ketter (2002) reported that euthymic patients with BD II performed better than manic or euthymic patients with BD I on fear recognition. Similarly, Derntl et al. (2009) found that subsyndromal BD II subjects displayed preserved task performance, whereas BD I exhibited defective emotion processing abilities. In contrast, Summers et al. (2006) found better performance favoring BD I depressed patients. However, there were significant IQ differences that may have confounded such results.

Only a handful of studies have investigated other clinical factors that might influence social cognitive functioning such as age at illness onset, history of psychotic symptoms, number of manic or depressive episodes, number of suicide attempts, subsyndromal symptoms, and exposure to medication. At present, no significant associations were found between ToM and duration of illness (Inoue et al., 2004; Bora et al., 2005; Wolf et al., 2010; Martino et al., 2011), history of psychotic symptoms (Bora et al., 2005; Lahera et al., 2008; Martino et al., 2011), number of previous episodes (Bora et al., 2005; Martino et al., 2011; Barrera et al., 2012) or subsyndromal symptomatology (Bora et al., 2005; Montag et al., 2010; Wolf et al., 2010; Martino et al., 2011). Only one small study (McKinnon et al., 2010) found that defective ToM was associated with subsyndromal symptoms and duration of illness. With regard to emotion recognition, no association was found between task performance and duration of illness (Bozikas et al., 2006; Vaskinn et al., 2007; Martino et al., 2011), history of psychotic symptoms (Martino et al., 2011) and number of previous episodes (Martino et al., 2011). Likewise, four out of seven articles reported nonsignificant associations between scores on mood rating scales and facial affect recognition (Harmer et al., 2002; Venn et al., 2004; Bozikas et al., 2006; Martino et al., 2011). Only two studies (Yurgelun-Todd et al., 2000; Hoertnagl et al., 2011) found a significant correlation between discrimination of facial affect expressions and level of depression, in the absence of correlations for manic symptoms, whilst Lembke and Ketter (2002) reported a negative correlation between recognition of sad faces and scores on the YMRS.

The effects of medication on social cognition have scarcely been studied. A small fMRI investigation by Jogia et al. (2008) documented that unmedicated BD patients performed similarly to controls on a task assessing the recognition of sadness. However, bipolar subjects exhibited diminished neural response in several brain regions involved in the processing of emotional states. After 12 weeks in treatment with lamotrigine, increased task related neural responses were seen in dorsomedial and ventrolateral

prefrontal cortical regions and subcortical regions (basal ganglia, thalamus, insula, brainstem). These findings support the idea that lamotrigine treatment may lead to a 'normalization' in key prefrontal regions associated with emotional self-regulation (2008).

Based on neuropsychological results, Bora et al. (2005) did not find any relationship between ToM and lithium dose. Similarly, Harmer et al. (2002) reported no significant association between emotion recognition and dosage of lithium, whereas Venn et al. (2004) did not find any differences among patients receiving antidepressants and those who were not. Likewise, Lahera et al. (2008) did not find any relation between mentalizing performance and medication status ('mood stabilizer + antipsychotic' and 'mood stabilizer'). By contrast, Martino et al. (2011) noted that usage of benzodiazepines was associated with poor Faux pas performance. The latter study also reported that the exposure to antipsychotics and benzodiazepines was inversely associated with fear recognition.

3.4. Social cognition and neurocognition in bipolar disorder

Even though it is yet not clear whether defective social cognition is mediated by neurocognitive impairments, very few attempts have been undertaken to assess the influence of neurocognitive variables into social cognitive outcome. Eight studies so far (Inoue et al., 2004; Bora et al., 2005; Olley et al., 2005; Vaskinn et al., 2007; Lahera et al., 2008; Montag et al., 2010; Wolf et al., 2010; Martino et al., 2011) have endeavored to investigate the influence of neurocognition on mentalizing performance. According to Olley et al. (2005), Bora et al. (2005), Lahera et al. (2008), and Martino et al. (2011), neurocognitive dysfunctions explain, at least partly, patient-control differences for ToM performance. In contrast, both Montag et al. (2010) and Wolf et al. (2010) observed defective mindreading performance even when co-varying out the effect of neurocognitive confounds, which may be seen as an argument for a rather specific nature of the social cognitive deficit. In keeping, Inoue et al. (2004) and Vaskinn et al. (2007) did not find any relationship between IQ and ToM or emotion processing respectively.

3.5. Social cognition and general functioning in bipolar disorder

An important clinical and research question regards whether social cognitive deficits are associated with less favorable functional status in bipolar patients as documented for other psychiatric disorders such as schizophrenia. To the best of our knowledge, only five studies have explored this relationship with mixed findings. It is worth noting, however, that different assessment instruments based on varying operationalizations of functional outcome have been used across studies. For instance, the Global Assessment of Functioning –GAF – (DSM-IV) is a global scale used by clinicians to rate subjectively the social, occupational, and psychological functioning of patients. The Social and Occupational Functioning Assessment Scale –SOFAS – (DSM IV) is similar to the former, but less focused on the overall severity of the patients' psychiatric symptoms and medical conditions. The Functioning Assessment Short Test –FAST – (Rosa et al., 2007) is an interviewer-administered scale that covers a wider variety of functional dimensions: autonomy, occupational functioning, cognitive functioning, financial issues, interpersonal relationships, and leisure time. Among self-administered measures, the World Health Organization Quality of Life Instrument –WHOQOL – (WHOQOL Group, 1998) assesses four domains: physical health, psychological, social relationships, and environment. Finally, the Life Functioning Questionnaire –LFQ – (Altshuler et al., 2002) assesses workplace, duties at home, leisure time with family, and leisure time with friends.

Olley et al. (2005) used the LFQ and the SOFAS to assess functionality in BD patients and found that none of the functional dimensions were associated with ToM. In keeping, Barrera et al. (2012) found no significant correlation between functional outcome (FAST scores) and ToM. Contrarily, Martino et al. (2011) documented that psychosocial functioning as assessed with the GAF correlated positively with performance on facial recognition of disgust and fear in BD patients, albeit these social cognitive variables were not independent predictors of functional outcome. Hoertnagl et al. (2011) reported a positive correlation between recognition of happiness and WHOQOL scores in a sample of euthymic subjects. To conclude, a recent study by Lahera et al. (2012) documented that low-functioning (FAST score > 11) euthymic BD patients showed a significant impairment in Faux pas and emotion recognition compared to a high-functioning (FAST score < 11) bipolar group.

4. Discussion

The present review sought to offer a look at the state of the art on social cognitive functioning in BD across the different phases of the illness. Notwithstanding the extensive body of evidence for deficits in distinct processes within social cognition, results are still inconclusive and many questions remain unanswered.

Among social cognitive domains, emotion processing is particularly relevant to BD, since impaired affect regulation is by definition a feature of the illness, and disturbances in the processing of emotional cues have been proposed as a factor in the development of bipolar affective symptoms (Yurgelun-Todd et al., 2000; Degabriele et al., 2011). Although findings have been quite inconsistent across studies, deficits in the appraisal of basic emotions have been noted in the three phases of BD. In keeping, recent evidence from a large functional magnetic resonance imaging (fMRI) study (Liu et al., 2012) revealed impaired response of the neural systems associated with acute mood symptoms – ventral anterior cingulate cortex, orbitofrontal cortex, and ventral striatum – to happy and neutral face stimuli in the three phases of BD. The presence of these findings across mood states is consistent with the notion of emotion processing dysfunctions being trait abnormalities of the disorder. Deficits in the appraisal of basic emotions in BD, however, do not appear to be generalized, but circumscribed to certain emotions. For instance, some studies have found diminished recognition of fear in the presence of spared overall accuracy (Venn et al., 2004; Martino et al., 2008, 2011). This is in line with the increasing evidence from neuropsychological and neuroimaging studies indicating that separable neural substrates may exist for the processing of different facial expressions (Broks et al., 1998; Adolphs et al., 1999; Calder et al., 2000). Nevertheless, very few investigations conducted so far have assessed the recognition of each emotion separately, making it difficult to draw a comprehensive picture of emotion processing deficits in BD.

An important finding of neuropsychological research is the presence of a mood congruent bias in the recognition of basic emotions (Lennox et al., 2004; Chen et al., 2006; Gray et al., 2006; Bermpohl et al., 2009). A fMRI study by Liu et al. (2012) showed that elevated mood states were associated with decreased right rostral prefrontal cortex activation to fearful and neutral faces, whereas depression was associated with increased left orbitofrontal cortex activation to fearful faces. Consistently, preliminary evidence has suggested that abnormalities in the processing of positive emotions may be associated with the development of elated mood (Degabriele et al., 2011, Rock et al., 2010). By means of neuropsychological assessment, Rock et al. (2010) showed that BD subjects with the bipolar phenotype, defined by high scores on the

Mood Disorder Questionnaire, exhibited enhanced recognition of positive emotions. By means of electrophysiological methods, Degabriele et al. (2011) examined two indices of face processing, namely the P100 and N170 components of the event related potential in patients with BD. Specifically, subjects with BD elicited facilitation for happy compared to sad faces as demonstrated by larger P100 amplitudes in response to this emotion. In accordance, Gruber et al. (2011) documented that euthymic BD patients displayed greater cardiac vagal tone in the processing of positive emotions compared to healthy controls. Vagal tone can be related to how people process relevant affective social information at the brain level (Dufey et al., 2011) and could be a useful approach to the study of emotion processing in bipolar patients.

With regard to ToM, neuropsychological evidence for impairments across the three phases of the illness is more consistent. Most studies using verbal tasks for the assessment of euthymic subjects have reported mindreading dysfunctions of moderate and large extent, whereas mild and non-significant dysfunctions were noted for Eyes tasks. Such differences may be attributed, at least partly, to the fact that ToM is not a monolithic function, but a set of processes that may be distinctly affected in BD. Indeed, it has been shown that affective and cognitive aspects of ToM are behaviorally distinguishable and subserved by different networks as demonstrated by evidence of selective deterioration in diverse clinical conditions – autism spectrum disorders, schizophrenia, sociopathy, and prefrontal brain damage – as well as imaging studies and psychophysiological findings in healthy control subjects (Vollm et al., 2006; Kalbe et al., 2007; Shamay-Tsoory and Aharon-Peretz, 2007; Kalbe et al., 2010). Moreover, it has been hypothesized (Abu-Akel and Shamay-Tsoory, 2011) that disruptions within the mentalizing network, at neurochemical or anatomical levels, would lead to varying degrees of mindreading impairment, thus indicating that ToM should not be regarded in dichotomous terms like an all-or-nothing capacity. Unfortunately, attempts to study dissected components of mentalizing abilities have been very scarce in BD. Finally, in remitted patients the question in regard to mentalizing deficits being specific or secondary to non-social cognitive impairments, deleterious medication effects, and subthreshold mood symptoms still remains open. At present, only a handful of studies have explored the influence of neurocognition on mindreading performance, yielding mixed results (Bora et al., 2005; Olley et al., 2005; Montag et al., 2010; Wolf et al., 2010; Martino et al., 2011). Nonetheless, it has been proposed that preserved executive functioning is needed to succeed at least in some variants of ToM tasks such as those requiring attributions about belief and knowledge, rather than those which require of empathizing and are mainly based on simulation processes (Kalbe et al., 2010). Hence, a more thorough assessment of the distinct dimensions within social cognition, together with traditional neuropsychological evaluation, may contribute to further understanding the possible influence of general cognition on bipolar patients' social cognitive performance.

A key finding of neuropsychological research is that emotion processing and ToM deficits are present even in euthymic BD subjects, which raises the question about these domains being candidate endophenotypes of the illness. BD is one of the most highly heritable medical disorders, with genetic influences accounting for 65–80% of variance in risk (Smoller and Finn, 2003). Nevertheless, its exact genetic profile remains unknown, which is due, in part, to not having identified intermediate phenotypical markers (or endophenotypes): traits that are more proximal to the genetic substrate than are diagnostic categories (Gottesman and Gould, 2003). To be considered endophenotypes, markers must be associated with the illness in the population, be heritable, co-segregate within families with illness, be state independent, and be more frequent in unaffected relatives of patients compared to the general population. The identification of neuropsychological abnormalities in unaffected first degree relatives of BD patients constitutes a critical approach in the search for possible heritable markers of the illness. Unaffected first-degree relatives are free from the effects of medication, acute symptoms and chronicity, and could therefore provide true picture of the mechanism of BD. Several neuropsychological functions have been proposed as potential endophenotypes for the disorder, and the strongest evidence is for verbal memory, sustained attention and executive functions, mainly response inhibition and set shifting (Arts et al., 2008; Bora et al., 2009). Social cognition has been scarcely studied as a possible endophenotype of BD. At present, there are no familiar studies of ToM in BD. With respect to emotion processing, preliminary evidence has shown abnormal performance in euthymic patients and subjects at risk for BD (Brotman et al., 2008). Furthermore, Surguladze et al. (2010) explored the neural correlates of emotion processing in BD subjects and their first degree relatives. They found a discrete pattern of exaggerated activity of medial prefrontal cortex and subcortical structures in response to either happy or fearful faces in euthymic patients and also in their unaffected relatives compared to controls. These results indicate that the overactivation of such brain structures in response to a facial emotion processing task may represent a neurobiological abnormality associated with genotypic variation conferring liability for BD. However, these findings need to be replicated.

The results yielded by the current review are limited by several methodological shortcomings that are common to investigations of cognitive aspects of BD such as poor between group matching on clinical/demographic variables, heterogeneous samples, varying definitions of euthymia, and low statistical power due to small samples in most studies. Another major concern relies on the fact that the extension and severity of cognitive impairments may be heterogeneous among euthymic bipolar patients as shown by some studies (Altshuler et al., 2004, 2008; Martino et al., 2008). These findings suggest that investigations reporting mean values of cognitive functioning in bipolar subjects may not be providing a comprehensive picture of cognition in BD, in which a subgroup of bipolar patients displays pronounced cognitive impairments whereas others exhibit preserved neuropsychological performance. Hence, a proper approach to studying social cognition in BD patients would be the inclusion of both a group and a multiple case series design, in which each individual's performance is compared with a normative sample. Another methodological limitation is that most investigations reviewed have assessed depressive symptomatology by means of the Hamilton Depression Rating Scale (Hamilton, 1960), an instrument that has been shown to be psychometrically and conceptually flawed (Bagby et al., 2004). Other weaknesses, however, are inherent to social cognition itself, since there is significant amount of variation between tests in the operationalization of social cognitive constructs, their complexity, the kind of stimuli used and the number of items included, which makes it difficult to compare results between studies. Hence, it is important to establish a consensus battery for the assessment of social cognition, including those tasks found to capture behavioral variance associated with defective social cognition in BD. According to recent meta-analytic findings (Samamé et al., 2012), only few ToM tasks, such as the Movie for the Assessment of Social Cognition, have been useful in showing medium-to-large patient-control differences, and there are not yet three studies showing moderate-large effect sizes using the same task in remitted subjects. Hence, we still lack recommended instruments for the assessment of BD patients' social cognitive performance that could inform therapeutic and pharmacological interventions. However, a number of neuropsychological measures may hold promise for reliably differentiating BD patients from healthy controls, but they require further study in this disorder (Table 3). These considerations reinforce the need for exploring

Table 3
Social-cognitive measures that may be potentially useful in detecting neuropsychological impairments in BD.

Neuropsychological test	Social cognitive domain	Studies including measure	Patient-control effect sizes for overall scores
Happé's Strange Stories Test (Happé, 1994)	Theory of mind	Lahera et al. (2008)	Cohen's $d=0.53$
Hinting Task (Corcoran et al., 1995)	Theory of mind	Bora et al. (2005)	Cohen's $d=0.68$
Movie for the Assessment of Social Cognition – MASC – (Dziobek et al., 2006)	Theory of mind	Montag et al. (2010)	Cohen's $d>0.8$
Theory of Mind Animation Task (Abell et al., 2000)	Theory of mind	Malhi et al. (2008)	Cohen's $d>0.8$
Emotion Hexagon (Calder et al., 1996)	Basic emotion recognition	Soeiro-de-Souza et al. (2012a,b)	Cohen's $d=0.68$
Facially Expressed Emotion Labeling – FEEL – (Kessler et al., 2002)	Basic emotion recognition	Hoertnagl et al. (2011)	Cohen's $d=0.77$
Kinney's Affect Matching Test – KAMT – (Kinney et al., (1995)	Basic emotion recognition	Bozikas et al. (2006)	Cohen's $d>0.8$

the relevance of these tasks to BD in future investigations and for developing other paradigms to assess social cognitive domains in bipolar patients. Furthermore, the influence of gestures, prosody, and other contextual information on social cognitive performance has been scarcely taken into account in neuropsychological research on BDs and other clinical samples. Investigations including more contextualized social cognition assessment instruments could possibly shed light on the nature of social cognitive functioning in BD.

To conclude, directions for future research are proposed. First, theory of mind and emotion processing should be further investigated by means of standardized task designs sensitive to subtle mindreading dysfunctions in order to identify which aspects of such broad domains are impaired and the magnitude of those impairments in the different phases of the illness. The relationship between different aspects within social cognition, general cognitive functioning and functional outcome remains to be ascertained. If social cognition deficits prove to be predictors of functional adjustment beyond neurocognitive deficits, they could be regarded as target areas for specific treatment and rehabilitation efforts aimed at arresting the social difficulties commonly observed in BD, which also impact on mood state. For instance, a preliminary hypothesis suggests that BDs biases in emotion recognition may be related to the emergence of affective symptoms and that tymoleptics work by remediating these biases. Then, such changes in bias, probably not accessible to subjective state, would be expected to lead to gradual changes in social reinforcement, behavior and mood over time (Harmer et al., 2009). Similarly, it has been suggested that social cognition may be associated with the sensitization phenomena related to bipolar disorder. Difficulties in 'reading' what is happening may expose subjects to stressful life events, which would trigger episodes and, finally, worsen the course of the disorder (Colom, 2012). Then, appropriate pharmacological and rehabilitation approaches should be aimed at arresting such roughening cycle. Moreover, knowing the pattern of social cognitive dysfunction across the three phases of BD and its neural correlates as assessed by means of neurophysiological and neuroimaging techniques would contribute to a better comprehension of the pathophysiology of the illness. Second, further investigation might serve to understand the possible contribution of clinical variables on the social cognitive performance of bipolar patients. There is some preliminary evidence indicating that BD II subjects could exhibit better emotion processing performance in comparison to BD I (Lembke and Ketter, 2002; Derntl et al., 2009). If BD II proves to display a more preserved social cognitive profile, the relationship between features associated to each diagnosis like psychosis and pharmacological variables should be investigated. For instance, a sizable body of literature has documented a negative impact of psychotropic medication on emotion processing and mindreading performance (Zangara et al., 2002; Mizrahi et al., 2006; Montag et al., 2008). Third, the relationship between age at onset and social cognitive profile should also be investigated. Indeed, it has been suggested that earlier onset of BD is related to worse ToM performance (Schenkel et al., 2008), since early mentalizing deficits may interfere with the development of social cognition abilities, with potentially long-term impact on social skills. BD with illness onset before 18 may represent a distinct, more severe and highly genetic form of the disorder associated with poor social adjustment (Carter et al., 2003; Craney and Geller, 2003). At present, there has not been any study exploring specifically the social cognitive performance of late-onset BD patients, since investigations of emotion processing and theory of mind in adult patients included an admixture of both early and late-onset subjects. Recent evidence summarized in a meta-analytic study (Samamé et al., 2013) suggests that neuropsychological performance may be worse in those patients experiencing illness onset after age 40 in comparison to those developing BD in early adulthood. The former considerations are in keeping with the proposal of establishing distinct bipolar subgroups according to age at onset (Faraone et al., 2004; Leboyer et al., 2005). In this context, future investigations should inform about social cognitive outcomes in the different subforms of the disorder. Fourth, the long-term course of social cognition in BD remains to be ascertained. Once identified those social cognitive areas with the largest magnitude of impairment, future endeavors should be aimed at exploring whether these deficits are static or progressive. As in cross-sectional studies, age at onset should be considered in the design of longitudinal studies of social cognition. For instance, late onset BD, which is associated with neurological illness, mainly cerebrovascular disease, and more pronounced cognitive deficits (Azorin et al., 2012), may be characterized by a distinct long-term course of social cognition. Hence, the admixture of patients with both late and early illness onset may not provide clear picture of the evolution of social cognitive features in the most highly genetic forms of the disorder. Finally, family studies exploring those social cognitive domains found to be impaired with medium-to-large effect size in remitted patients are necessary. This approach would contribute to determining whether impaired social cognition is a trait marker and candidate phenotypic subtype that could facilitate research on the underlying genetics of the illness.

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