The forgotten affective route of social cognition in patients with bipolar disorders

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Abstract
Social cognition (SC) research in bipolar disorders (BD) has provided evidence about deficits in different phases of the illness. Most of the studies have focused on two aspects of SC: theory of mind and emotion recognition. However, according to influential models of social neuroscience, two aspects of understanding others need to be distinguished: the cognitive (theory of mind and emotion recognition) and the affective route (empathy and compassion) of SC. We aimed to determine whether individuals with BD significantly differ from healthy controls on measures of the affective route of SC according to the available evidence. We conduct a narrative review of original research based on a social neuroscience model of SC. BD is associated with alterations of the affective route of SC during acute episodes and remission. During mania and subthreshold depression, an increase in empathy (“over-empathizing”) and discomfort (empathy) has been reported, respectively. A pattern of high empathic distress and low compassion appears during remission. This article is the first to review the evidence on the affective route of SC in BD, revealing trait and state alterations. We emphasize the need to consider this affective dimension of SC in future research, to design more specific interventions in BD patients.

Keywords
bipolar disorder, empathy, affect, depression, compassion

Date received: 5 May 2022; accepted: 11 October 2022

Introduction
Although the presence of mood symptoms is the main characteristic of bipolar disorders (BD), remission of these symptoms does not necessarily lead to adequate levels of functionality (Haro et al., 2011; Sánchez-Moreno et al., 2009).

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This insight has encouraged the study of other clinical measures related to functional outcome. These studies revealed that neurocognitive deficits (i.e., executive function, memory, verbal learning, attention, and processing speed) may cause perpetuating psychosocial dysfunction regardless of affective symptomatology (Baune & Malhi, 2015; Bowie et al., 2010; Burdick et al., 2010; Jaeger et al., 2007; O’Shea et al., 2010; Tabarés-Seisdedos et al., 2008; Torres et al., 2011). In addition, other studies have showed that social cognition (SC) plays an important role in psychosocial functioning in bipolar patients (Hajnal et al., 2010; Lahera et al., 2009; Martino et al., 2011; Montag et al., 2010; van Rheenen & Rossell, 2014).

SC, understood as the “psychological processes that are involved in the perception, encoding, storage, retrieval, and regulation of information about other people and ourselves” (Green et al., 2015), has been studied across several research levels, providing information from basic research to clinical investigations, indicating the translational potential of these processes (Gur & Gur, 2016). In the field of BD, several articles have focused on deficits in SC, leading to the generation of distinct hypotheses about the association between such deficits and the phases of the illness (Bora et al., 2016; Rocca et al., 2009; Samamé, 2013; Samamé et al., 2012). In the same way, researchers have used these data to discuss the specificity of social cognitive impairment in both bipolar and schizophrenia patients (Bora & Pantelis, 2016; Lee et al., 2013; Martino et al., 2017), the stability of SC functioning (Martino et al., 2016), and the status of such functioning as a marker of vulnerability of a potential endophenotype (Bora & Özerdem, 2017). Likewise, other hypotheses have emerged suggesting an association with hormonal variables, particularly oxytocin (Pérez-Rodríguez et al., 2015), relationships with neural correlates (Chen et al., 2006), or even associations with genetic variants (Soeiro-De-Souza et al., 2012). So far, most of these studies seem to focus mainly on two dimensions of SC, namely, theory of mind (ToM) and emotion recognition. The other three dimensions of SC proposed by the National Institute of Mental Health are social knowledge, attributional bias, and social perception, based on the schizophrenia model (Green et al., 2008), which exhibits differences with respect to the phenomena observed in BD (Lee et al., 2013). Empathy itself has not been considered in one of the five dimensions. However, the boundaries between these categories are imprecise and the research on empathy in schizophrenia is preliminary (Green et al., 2008, 2019; Vaskinn & Horan, 2020), which may explain its exclusion from this taxonomy. Besides, this classification stresses the cognitive component itself of SC. The Institute proposal (emerged from a consensus-building meeting) emphasized the need to build bridges between clinical researchers, neuroscientists, and social scientists, in order to address the inconsistent terminology and differences in the way SC is measured. The present review builds on the conceptual framework provided by one of the influential social neuroscience models distinguishing different aspects of SC, proposed by Tania Singer (2006, 2012).

The “Singer model” distinguishes two different routes to understanding others (Singer, 2006, 2012). The cognitive route of SC, which involves the terms “theory of mind” (ToM) or “mentalizing,” encompasses the ability to infer and reason about the beliefs, thoughts, or emotions of others (Frith & Frith, 2005). Based on this model, the cognitive route entails reasoning about others’ mental and affective states, processes also known as “cognitive ToM” and “affective ToM” (or “cognitive empathy”), respectively. According to this model, “emotion recognition” is another term used in the literature that should be considered part of the cognitive route of SC. The affective route of SC has been studied under the terms “empathy” and “compassion.” The former has been defined as sharing another’s emotional state while being aware that the other is the source of the emotion (de Vignemont & Singer, 2006); in other words, in empathy one feels with someone, but one does not confuse oneself with the other. When this distinction is not present, researchers speak of “emotion contagion,” a precursor of empathy (Singer & Klimecki, 2014). Other terms used synonymously with empathy in some clinical research are “affective empathy,” “emotional empathy,” (Decety & Jackson, 2006) and “experience sharing” (Green et al., 2015). Compassion is characterized by feelings of warmth, concern, and care for the other, along with a strong motivation to improve the other person’s well-being (Singer & Klimecki, 2014). Comparatively, compassion is feeling for and not feeling with the other.

On a behavioral level, this model proposes different empathic reactions to the suffering of others. In healthy subjects, exposure to the distress and suffering of others can lead to distinct emotional reactions: “empathic distress,” which refers to a strong aversive and self-oriented response to the suffering of others, resulting in negative feelings and associated with negative health outcomes (burnout), or “compassionate responses,” based on other positive feelings (warmth, concern, and care for the other) and the activation of prosocial motivation and leading to better health outcomes (Singer & Klimecki, 2014). Table 1 shows terms used in the literature to describe different cognitive and affective aspects of SC. These processes have been studied in individuals with BD during depressive and manic episode as well as euthymia, allowing the measuring of “trait alterations” and “state alterations.”

Neural correlates of the cognitive and the affective route of SC have been studied, providing evidence that these processes represent different abilities. The cognitive route has been linked to activation in the tempo-parietal junction, temporal poles, the medial prefrontal cortex, and the pre-cuneus/posterior cingulate (Schurz et al., 2014). In this sense, it is interesting to consider that some studies...
corroborate a partial neurobiological independence between affective ToM, related to regions such as the orbitofrontal cortex and ventromedial prefrontal cortex (Eslinger, 1998; Shamay-Tsoory et al., 2005), and cognitive ToM, in which areas such as the dorsolateral prefrontal cortex would participate (Abu-Akel & Shamay-Tsoory, 2011). Indeed, one study verified that repetitive transcranial magnetic stimulation over the right dorsolateral prefrontal cortex induced a selective effect on cognitive but not affective ToM (Kalbe et al., 2010). Therefore, the interdependence and putative implication of affective ToM in the affective route of SC is plausible and a matter of discussion.

Within the affective route, the “emotional component” of empathy is associated with more unconscious and automatic activity related with the anterior insula, inferior parietal lobule, inferior frontal gyrus, and the middle anterior cingulate cortex (Fan et al., 2011). On the other hand, as a dimension of the cognitive route, cognitive empathy correlates with a network comprising the ventromedial and dorsomedial prefrontal cortex, anterior midcingulate cortex, temporo-parietal junction, and medial temporal lobe, which are involved in attribution of mental states, ToM processes, and perspective-taking (Shamay-Tsoory et al., 2009a). Compassion relies on a different neural network, comprising areas linked to positive affect such as the ventral striatum (Klimecki et al., 2013a). Moreover, recent evidence, by assessing both functions simultaneously, has corroborated that people’s capacities for empathizing (affective route) and mentalizing (cognitive route) are independent, at both the behavioral and the neural level (Kanske et al., 2015). Even more so, training compassion or empathy leads to differential plasticity in neural networks, supporting the relevant distinction between both components of the affective route of SC (Klimecki et al., 2013b).

Although the Singer model has emerged from healthy subject data, this model will help to identify evidence gaps in the literature. Starting from a specific model will help to avoid terminological confusion. Different terms are used in the field to describe similar processes, and similar terms are used to describe clearly different processes. Clarification of the terminology will allow us to more precisely understand which specific aspect of SC the respective studies have addressed and how findings of different studies are related to each other.

Drawing on the Singer model, it becomes clear that most of the articles on SC in BD have offered data and hypotheses within the cognitive route of SC. Furthermore, previous authors have thoroughly reviewed the cognitive route of SC (Bora et al., 2016; Rocca et al., 2009; Samamé, 2013; Samamé et al., 2012). In the present review, we are adding to these previous reviews by focusing on the affective route of SC. The aim of the present article was to determine whether individuals with BD significantly differ from healthy control subjects in affective SC measures, in order to provide new data for a more comprehensive discussion about SC deficits and their clinical relevance in patients with BD.

### Materials and methods

We conducted a search of the literature to identify studies about the affective route of SC (empathy and compassion) in BD using online databases (PubMed/Medline, PsychInfo, Google Scholar, and the Cochrane Library); the last search was conducted in March 2022. We used MeSH terms such as “bipolar disorder,” “empathy,” “affect,” and “depression.” We included uncontrolled language terms such as “affective empathy,” “emotional empathy,” “experience sharing,” “compassion,” and “mania.” Studies were included in the review if they met the following criteria: primary (any methodological design) or secondary (systematic reviews with or without meta-analysis) research articles reported results in the field of the affective route of SC (Singer, 2006, 2012; Singer & Klimecki, 2014); used standardized diagnostic criteria to determine BD diagnoses; included a healthy comparison group or patients with other psychiatric diagnoses (e.g., schizophrenia); and provided information about patients’ mood state (mania, depression, or euthymia). Studies were excluded when they had investigated “cognitive empathy,” which is considered synonymous with affective ToM, which is part of the cognitive route of SC in the Singer model (Singer, 2006, 2012; Singer & Klimecki, 2014). Since this review exclusively focuses on the affective route of SC, these studies were not

### Table 1. Different terms used to describe the cognitive and affective routes of SC.

| Cognitive route of SC | Affective route of SC |
|-----------------------|-----------------------|
| • Mentalizing or ToM (affective ToM or cognitive empathy and cognitive ToM) (Bora et al., 2016; Fan et al., 2011; Martino et al., 2011; Montag et al., 2010)  | • Empathy, affective empathy, emotional empathy, or experience sharing (Decety & Jackson, 2006; Green et al., 2015) |
| • Emotion recognition (Green et al., 2008)  | • Empathic distress (Klimecki et al., 2013a) |
| • Social knowledge (Green et al., 2008)  | • Compassion or compassionate responses (Singer & Klimecki, 2014) |
| • Attributional bias (Green et al., 2008)  |  |
| • Social perception (Green et al., 2008)  |  |
considered here. Two authors independently screen the titles and abstracts of all retrieved records for potential eligibility. After retrieval of full-text study, they independently assessed and classified them. Any disagreements were resolved through discussion or by consultation with a third author (first author).

**Results**

We identified 73 articles. The most common reason for exclusion was the use of the term “empathy” to refer to cognitive empathy tasks or the emotion processing paradigm, both of which concern the cognitive route of SC in the Singer model. Only eight studies included some affective route indices in patients with BD (Table 2).

**Findings about measurement of the affective route**

Different instruments have been used to evaluate processes of the affective route of SC in BD patients. Most studies in euthymic BD patients used the Interpersonal Reactivity Index, an individual difference measure of empathy based on a multidimensional approach (good internal consistency and correlates with other measures of empathy, supporting the construct validity of the measure) (Davis, 1980, 1983). Two subscales of this questionnaire measure respondents’ emotional reactions: “Empathic Concern,” a subscale that assesses “other-oriented” feelings of sympathy and concern for unfortunate others, in other words, “compassion”; and “Personal distress,” a sub-scale that measures “self-oriented” feelings of personal anxiety and unease in tense interpersonal settings, which refers to “empathic distress” in the Singer model. It is plausible to argue that exposure to negatively valenced stimuli poses a distinct challenge and is clearly more difficult to cope with. In this regard, the Interpersonal Reactivity Index makes it possible to differentiate between two types of empathic response (Figure 1): “empathic distress” and “compassion” (Batson, 2009).

The “state alterations” were observed mainly through the Multifaceted Empathy Test, a naturalistic measure of empathy that allows the separate assessment of cognitive and emotional aspects of empathic functioning (internal consistency ranging from 0.71 to 0.92 and highly satisfactory convergent and divergent validity) (Dziobek et al., 2008).

### Table 2. Alterations in the affective route of SC in BD patients.

| Study | BD | HC | SZ | Affective route task | Clinical state (clinical instrument) | Results |
|-------|----|----|----|----------------------|--------------------------------------|---------|
| 1. Wiener et al. (2011) | 20 | 40 | 20 | Multifaceted Empathy Test | Subthreshold mania (YMRS/HAM-D) | Increased empathy in BD patients with subthreshold mania symptoms. |
| 2. Gruber et al. (2009) | 55 | 32 | — | Interpersonal reactivity Index | Subthreshold depression (MADRS/YMRS) | BD patients reported higher compassion compared to HC. |
| 3. Bodnar et al. (2017) | 50 | 25 | — | Interpersonal reactivity Index | Euthymia (SUM.M/SUM.D) | No differences in empathy during depression compared with HC. |
| 4. Yang et al. (2017) | 30 | 23 | — | Multifaceted Empathy Test | Mania depression (YMRS/HAM-D) | Increased empathy during manic episode in BD patients. |
| 5. Báez et al. (2013) | 15 | 30 | 15 | Empathy for pain Task | Euthymia (SUM.M/SUM.D) | BD patients reported higher compassion. |
| 6. Cusi et al. (2010) | 20 | 20 | — | Dispositional positive Emotion Scale (DPES) | Euthymia subthreshold depression (HAM-D/YMRS) | BD patients exhibited higher ratings of discomfort (empathy) compared to HC. |
| 7. Seidel et al. (2012) | 21 | 21 | — | Empathy for pain Task | Euthymia subthreshold depression (MADRS/YMRS) | BD patients reported higher empathic distress ratings compared with HC. |
| 8. Shamay-Tsoory et al. (2009a) | 19 | 20 | — | Multifaceted Empathy Test | Euthymia (HAM-D/YMRS) | BD patients scored significantly higher than controls on empathy, reporting higher empathic distress ratings compared with HC. |

BD: bipolar disorders; HC: healthy controls; SZ: schizophrenia; YMRS: Young Mania Rating Scale; HAM-D: Hamilton Rating Scale of Depression; MADRS: Montgomery–Asberg Depression Rating Scale; SUM.M: Mood Elevation Subscale of the Clinical Monitoring Form; SUM.D: Depression Subscale of the Clinical Monitoring Form; BRMS: Bech–Rafaelsen Mania Scale, n.s.: no statistical significance.
According with the aims of this review, we focus exclusively on the part of this instrument that reflects the degree of “emotional empathy” (“empathy” in the Singer model) experienced by an individual exposed to visual stimuli, consisting of a series of photographs, most of which depict people in emotionally charged situations. Participants must answer the following questions: “To what extent are you feeling like the person in the picture?” and “How much are you moved by the picture?” which assess explicit and implicit empathy, respectively (Dziobek et al., 2008). This procedure yields a quantitative measure of the degree of empathy reported in a behavioral test, for positive and negative stimuli ("degree of empathy experience" in Figure 1). Other measurement instruments used in the studies to appraise the SC were the Dispositional Positive Emotional Scale (good internal consistency; \( \alpha = 0.84 \) for compassion) (Gruber et al., 2009), and the Empathy Pain Task (internal consistency for valence and arousal of 0.82) (Backs et al., 2005).

The affective route alterations in patients with BD

Figure 1 illustrates the alterations observed in the affective route of SC in BD patients. The scheme distinguishes state or trait alterations and responses to positively and negatively valenced stimuli. The studies identified both trait and state alterations through behavioral assessment instruments and self-report measures. In the case of trait alterations, BD patients (euthymic or subsyndromal status) exposed to negatively valenced stimuli, scored high in “empathic distress” in comparison with healthy control subjects (Báez et al., 2013; Cusi et al., 2010; Demtl et al., 2012; Seidel et al., 2012; Shamay-Tsoory et al., 2009b), reflecting the degree to which they feel uncomfortable when confronted with the suffering of others, and scored low in “compassion” (Dermel et al., 2012; Gruber et al., 2009), showing their tendency to feel less concern regarding unfortunate others. Within state alterations, the most relevant result regarding empathy occurs mainly during manic episodes (Bodnar & Rybakowski, 2017; Wiener et al., 2011; Yang et al., 2017): an increase in empathy (“high degree of empathy experience”) in comparison with control subjects, regardless of the valence of the stimulus presented. This phenomenon was observed through the Multifaceted Empathy Test, in both implicit and explicit measures of empathy (Dziobek et al., 2008). The state-dependent phenomenon was confirmed by a significant correlation between empathy scores and the intensity of manic symptoms (Bodnar & Rybakowski, 2017). In contrast, the measures of empathy in depressed patients did not differ from those of healthy control subjects (Bodnar & Rybakowski, 2017). Only one study measured the empathic response type in bipolar patients with manic symptoms, reporting lower “compassion” ratings (Yang et al., 2017). Figure 1 shows a schematic overview of alterations of the affective SC in BD patients.

The affective route and functional outcomes

Despite their clinical relevance, relationships between functional outcomes and the affective route alterations have
received little attention by researchers. Only one study measured the association between these two variables, finding a significant correlation between empathy and various psychosocial domains (Cusi et al., 2010). Specifically, individuals who displayed high “empathic distress” in negative social situations showed reduced social functioning. Moreover, individuals who scored lower on the compassion scale also showed reduced functioning on the social/leisure activities scale (Cusi et al., 2010). These results are consistent with the idea proposed by Singer that high empathic distress and low compassion most likely give rise to negative health outcomes (Singer & Klimecki, 2014).

The relationship between affective route and cognitive route

It is important to consider the relationship between alterations in the cognitive and the affective route to achieve a more comprehensive view on SC in BD patients. Seven studies included cognitive route tasks of SC (ToM or emotion processing). Most of these studies reported deficits in several domains of the cognitive route when comparing BD patients and healthy control subjects (Baez et al., 2013; Bodnar & Rybakowski, 2017; Cusi et al., 2010; Derntl et al., 2012; Seidel et al., 2012; Shamay-Tsoory et al., 2009b); however, only few studies have tested for correlations between cognitive and affective SC alterations. Shamay-Tsoory et al. reported that empathy did not correlate with cognitive ToM (r 0.341, n.s.) nor with affective ToM (r 0.291, n.s.) (Shamay-Tsoory et al., 2009b). Another study found alterations in the affective route controlling for the cognitive route (i.e., emotion recognition and perspective-taking), suggesting alterations of the affective route may exist independently of alterations in the cognitive route (Derntl et al., 2012).

Starting point of the present review was the Singer model distinguishing different aspects of cognitive and affective routes of social understanding. Relying on this model, we focused on affective route alterations in BD. We identified a pattern of “high empathic distress” and “low compassion” during euthymia and subsyndromal states (trait alterations). On the other hand, studies reported “increased empathy” (“over-empathizing”) and “low compassion” during mania (state alterations).

Discussion

SC research has drawn great attention in BD, because it plays a critical role in psychosocial functioning in this and other patient groups (Hajnal et al., 2010; Lahera et al., 2009; Martino et al., 2011; Montag et al., 2010; van Rheenen & Rossell, 2014). Most studies in BD have focused on two aspects of SC, namely, ToM and emotion recognition (Bora et al., 2016; Rocca et al., 2009; Samamé, 2013; Samamé et al., 2012). However, besides this cognitive route (cognitive ToM, affective ToM and emotion recognition) of SC, an affective route (empathy and compassion) needs to be considered (Kanske et al., 2015; Klimecki et al., 2013a, 2013b; Singer, 2006, 2012; Singer & Klimecki, 2014). To date, reviews on SC in BD have ignored this affective route.

In the present article, we review the available patient data in light of a theoretical model developed in the field of social neuroscience. We found that BD is associated with alterations of the affective route of SC during both acute episodes and remission. These data seem relevant in order to promote a more detailed discussion about alterations in SC and their clinical relevance in patients with BD.

The affective route alterations in BD

BD patients showed state alterations during the presence of manic symptoms, comprising a pattern of increased empathy (over-empathizing) regardless of the emotional valence of the stimulus and low compassion. “Over-empathizing” may cause excessive, inappropriate reactions in social interaction (Bodnar & Rybakowski, 2017), which may lead to disturbances in social functioning. In this line, a study conducted by M’Bailara et al. (2009), concluded that euthymic BD patients report higher levels of emotional reactivity in response to neutral stimuli. The authors discussed the consideration of this emotional hyper-reactivity as an endophenotype in BD and stressed its importance since BD patients not only show an increased risk of recurrence when facing major life events, but also with minor life events. These findings align with the clinical importance of over-empathizing, since it would allow to distinguish people at risk of presenting BD. It is worth noting that this finding is under several descriptions of manic features based on different theories. Bleuler’s classical phenomenological description, through the concept of “syntony” (1911), refers to the “tendency of the manic to vibrate in unison with the environment” (Widakowich, 2015). In line with this, psychodynamic studies have found an “excessive permeability to the environment, a porosity of limits, and excessive sensoriality and affectivity in bipolar patients” by means of projective tests (Sagelas-Granval, 2004). The problem of the great heterogeneity of diagnostic categories in psychiatry is recognized. This also affects narrower phenotypes such as mania, whose clinical presentation fluctuates between euphoric, mixed, and dysphoric states. Therefore, it is possible to hypothesize that the functioning of the SC will also be variable in relation to the predominant mood, being more likely to find increased empathy in euphoric states. The “over-empathizing” phenomenon could relate to disturbances of emotion regulation (Gruber, 2011), given the high demand on the ability to regulate and modulate the emotional experience (Decety & Lamm, 2006). Neuroscience research
has demonstrated that the amygdala and the insula play a key role in normal emotion processing and that the medial and lateral regions of the prefrontal cortex take part in mood regulation (Baker et al., 1997; Northoff et al., 2000). Studies on mania have reported an attenuated ventrolateral prefrontal cortex activity and, at the same time, heightened amygdala and insula activity (Townsend & Altshuler, 2012), which may result from deficient prefrontal inhibition. Since amygdala and insula have also been implicated in empathizing (Engen & Singer, 2013), the present finding of “over-empathizing” in mania could be interpreted in the context of the emotion regulation model of BD. Specifically, exaggerated emotional responses to others, expressed through a dysfunctional empathic overreaction, could be related to prefrontal hypoactivation and corresponding amygdala and insula hyperactivation during mania.

Báez et al. (2013) corroborated that BD patients in euthymia and depression exhibit impairments in empathy that may be dependent on emotional processing; particularly, depressive symptoms play an important role through the variation of discomfort judgments. Empathizing with suffering of someone can lead to different responses. To prevent an excessive sharing of suffering that may turn into distress (“empathic distress”), people may respond to the suffering of others through a “healthier” response, namely, “compassion” (Singer & Klimecki, 2014). BD patients showed trait alterations of the affective route of SC in the context of negatively valenced stimuli, with data supporting a pattern of high “empathic distress” and low “compassion.” This evidence could reflect a greater tendency towards having self-oriented feelings of anxiety and discomfort (possibly mediated by declines in executive functioning and memory resources in BD (Cusi et al., 2010)) in response to tense interpersonal settings in patients with BD (Shamay-Tsoory et al., 2009b). This finding may be interpreted in light of the emotional dysregulation in BD patients (van Rheenen et al., 2014) and the evidence about a pattern of chronic ventrolateral prefrontal cortex hypoactivation, even during euthymia (Blumberg et al., 2003). Indeed, the decrease in positive emotions during euthymia has been associated with the neuroprogression of bipolar illness. This fact is of great clinical relevance, since as it was verified in the study by Gruber et al. (2009), the presence of compassion predicted less severe manic episodes, a fact that could be due to the construction of protective support networks that promote patient care during the appearance of manic symptoms. Likewise, Cusi et al. (2010) suggest that alterations in empathic responding are associated with more severe symptomatology in BD patients. The authors analyzed a group of BD patients in euthymia and depression, concluding that alterations in the empathic response would be a trait rather than a state phenomenon in BD patients. However, Seidel et al. (2012) found in euthymic BD patients that the greater the severity of the residual depressive symptoms, the greater the alteration of the ability to take the perspective of another person in an emotional situation, namely, an empathic competency. In the case of unipolar depression, studies that analyze the relationship between alterations in empathy (as a trait and as a state) and depression are scarce and their results controversial (Rum & Perry, 2020; Schreiter et al., 2013).

The affective route and functional outcomes

BD is associated with functional deficits in a wide variety of areas including impairments in work and employment (Hirschfeld et al., 2003), as well as in the social (Simon, 2003), psychological, physical, and environmental domains (Michalak et al., 2007), persisting even after symptomatic recovery (Zarate et al., 2000). Given the role of SC in facilitating social interactions and modulating behaviors essential to a healthy psychosocial outcome, deficits in SC are likely to contribute to impaired psychosocial functioning in BD (van Rheenen & Rossell, 2014). It seems worthwhile to include functionality outcome on SC research, considering the clinical relevance; however, there is scarce evidence about the relationship between the affective route of SC and functional outcomes. Only one study, included in the present review, showed that high empathic distress in negative social situations was related to difficulties maintaining successful familial and social relationships as well as to social functioning deficits in occupational and leisure activities (Cusi et al., 2010).

The relationship between the routes of SC

Singer et al. developed a paradigm (i.e., the EmpaToM) that allows studying the affective and cognitive route of SC simultaneously in one experiment. They found that in highly emotional situations, empathic sharing (affective route) can inhibit mentalizing-related activity and thereby harm mentalizing performance (cognitive route) in healthy people (Kanske et al., 2016). Considering these data and the reviewed affective route alterations in BD, the question arises: How alterations of the affective and cognitive route of SC are related to each other in BD? While first evidence suggests that alterations of the affective route of SC occur independently of the cognitive route in BD (Dernstl et al., 2012; Shamay-Tsoory et al., 2009b), future studies may include measures of both routes in order to improve our understanding of the interplay of affective and cognitive SC in BD patients. From another viewpoint, Schurz et al. (2021) conducted a meta-analysis of the results from neuroimaging studies, and highlighted three clusters of cognitive and affective processes: those mainly cognitive, those predominantly affective and a third group represented by a pathway combined of the two previous groups. This new cluster would offer a less biased alternative to the more.
generalized nomenclature to designate processes such as ToM and empathy, since the coactivation of cognitive and affective phenomena would constitute the most plausible model, being observed in multiple paradigms that evaluate SC.

**Therapeutic implications**

The findings reviewed here may help to modify and improve psychosocial interventions in patients with BD. Specifically, interventions may place particular emphasis on enhancing “low compassionate responses” and reducing “high empathic distress.” For this purpose, one may resort to interventions developed to foster empathic and compassion skills in non-psychiatric populations and shown to lead to plastic changes in neural networks in healthy individuals (Klimecki et al., 2013b). At the psychological level, compassion training had a beneficial impact on self-reported feelings of positive affect, personal resources, and well-being in healthy individuals (Fredrickson et al., 2008). In the same vein, long-term mindfulness meditation has been associated with increased self-regulation and decreased distress (Hölzel et al., 2011; Laneri et al., 2017), providing an adaptive mechanism for coping with distress because of the empathic sharing of others’ suffering, thereby possibly enabling compassionate behavior (Deckersbach et al., 2012; Edge et al., 2013; Murray et al., 2017). In clinical samples, patients with borderline personality disorder showed significant improvements in the severity of borderline symptoms after a loving-kindness and compassion meditation training (Feliu-Soler et al., 2017). A network meta-analysis of 46 randomized clinical trials (Nijman et al., 2020) analyzed the effect of social cognition training for people with schizophrenia spectrum disorders, corroborating a positive impact in dimensions such as emotion and social perception, but the components of the affective route were not measured. In BD patients, this intervention has been much less studied. In a small-scale randomized clinical trial, Lahera et al. (2013) found that the therapy would improve SC, but measures of empathy or compassion were not considered. The same intervention was studied by Zhang et al. (2019), but no measures of SC were assessed. Progress in psychotherapy could be related with the developing of interventions from a more comprehensive model of the SC in BD patients, including the alterations of the affective route.

**Future aims and conclusions**

Various neuropsychiatric disorders have been shown to involve social cognitive impairments, and they differ regarding the pattern of deficits observed and their developmental courses (Green et al., 2015). Our data emphasize the need to stronger consider the affective dimension of SC in future research in BD patients.

To date, no study has investigated the empathic response type to positive contents in BD patients. Likewise, there is no data about the impact of empathy or compassion training on clinical outcomes in patients with BD. In the same direction, there is a need for further research on the association between the routes of SC and functional outcomes, considering the clinical relevance. Besides, research on compassion in BD is very scarce, which is probably related to the fact that the conceptualization and operationalization of the construct is very incipient in clinical and neuroscientific research.

One of the major limitations of the present article was the scarce evidence available on the affective route of SC. Similarily, the available data have emerged from studies that have used heterogeneous clinical samples, examined with a variety of mood symptomatology assessment methods. The diversity of instruments used to operationalize the SC construct, along with the lack of prospective cohort studies, also make up aspects that limit the discussion. In the light of the foregoing, the development of appropriate test instruments under current theoretical models and clinical plausibility would allow a better understanding of the specificity of alterations in SC in BD patients. In addition, we did not consider the medication status of the participants, a factor that could to a certain extent alter the SC measurements.

In conclusion, our review shows alterations of the affective route of SC during both acute episodes and remission. Incipient evidence demonstrates an increase in empathy (“over-empathizing”) during mania as the main state alteration. On the other hand, high “empathic distress” and low “compassion” appear during remission (trait alterations). Conducting research within a coherent and well-documented conceptual framework, attempting to integrate the evidence provided by social neuroscience, will not only increase the depth of our analysis of the SC, but could also open up new perspectives for designing more specific therapeutic interventions, thus improving functioning and quality of life in BD patients.

**Concluding remarks**

Social cognition research in bipolar disorder has provided evidence about deficits in different phases of the illness. However, to date, there is no study that synthesizes the findings concerning the alterations of the affective route of social cognition in bipolar disorder. We conducted a narrative review and a critical analysis based on the Singer’s neuroscience model of social cognition, identifying a pattern of “high empathic distress” and “low compassion” during euthymia and subsyndromal states (trait alterations). On the other hand, studies reported “increased empathy” (“over-empathizing”) and “low compassion” during mania...
(state alterations). We emphasize research and clinical analysis of the clinical dimensions in bipolar disorder. Incorporating affective aspects of social cognition could open up new perspectives for designing more specific therapeutic interventions in patients with bipolar disorder. Progress in psychotherapy should consider a more comprehensive model of social cognition in bipolar patients, including the alterations of the affective route.

Declaration of conflicting interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The study receive funding from ANID - Millennium Science Initiative Program / Millennium Institute for Research on Depression and Personality-MIDAP ICS13_005.

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Supplemental Material
Supplemental material for this article is available online.

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