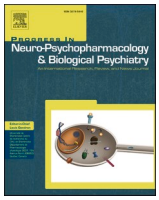
Progress in Neuropsychopharmacology & Biological Psychiatry 127 (2023) 110847

Contents lists available at ScienceDirect

Progress in Neuropsychopharmacology & Biological Psychiatry

journal homepage: www.elsevier.com/locate/pnp



Differences in facial emotion recognition between bipolar disorder and other clinical populations: A systematic review and meta-analysis

Michele De Prisco [a,b,c,d,1], Vincenzo Oliva [a,b,c,e,1], Giovanna Fico [a,b,c], Laura Montejo [a,b,c,d], Chiara Possidente [b,c,e], Lorenzo Bracco [b,c,f], Lydia Fortea [a,g], Gerard Anmella [a,b,c], Diego Hidalgo-Mazzei [a,b,c], Michele Fornaro [h], Andrea de Bartolomeis [h], Alessandro Serretti [e], Andrea Murru [a,b,c], Eduard Vieta [a,b,c,d,*], Joaquim Radua [d,g,i,j]

[a] Departament de Medicina, Facultat de Medicina i Ciències de la Salut, Universitat de Barcelona (UB), c. Casanova, 143, 08036 Barcelona, Spain
[b] Bipolar and Depressive Disorders Unit, Hospital Clinic de Barcelona, c. Villarroel, 170, 08036 Barcelona, Spain
[c] Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), c. Villarroel, 170, 08036 Barcelona, Spain
[d] Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Instituto de Salud Carlos III, Madrid, Spain
[e] Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy
[f] Department of Pathophysiology and Transplantation, University of Milan, 20122 Milan, Italy
[g] Imaging of Mood- and Anxiety-Related Disorders (IMARD) Group, IDIBAPS, Barcelona, Spain
[h] Section of Psychiatry, Department of Neuroscience, Reproductive Science and Odontostomatology Federico II University of Naples, Naples, Italy
[i] Early Psychosis: Interventions and Clinical-Detection (EPIC) Lab, Department of Psychosis Studies, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, United Kingdom
[j] Centre for Psychiatric Research and Education, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

ARTICLE INFO

Keywords:
Bipolar disorder
Facial expression recognition
Schizophrenia
Major depressive disorder
Sadness

ABSTRACT

Facial emotion (or expression) recognition (FER) is a domain of affective cognition impaired across various psychiatric conditions, including bipolar disorder (BD). We conducted a systematic review and meta-analysis searching for eligible articles published from inception to April 26, 2023, in PubMed/MEDLINE, Scopus, EMBASE, and PsycINFO to examine whether and to what extent FER would differ between people with BD and those with other mental disorders. Thirty-three studies comparing 1506 BD patients with 1973 clinical controls were included in the present systematic review, and twenty-six of them were analyzed in random-effects meta-analyses exploring the discrepancies in discriminating or identifying emotional stimuli at a general and specific level. Individuals with BD were more accurate in identifying each type of emotion during a FER task compared to individuals diagnosed with schizophrenia (SCZ) (SMD = 0.27; *p*-value = 0.006), with specific differences in the perception of anger (SMD = 0.46; p-value = 1.19e-06), fear (SMD = 0.38; p-value = 8.2e-04), and sadness (SMD = 0.33; p-value = 0.026). In contrast, BD patients were less accurate than individuals with major depressive disorder (MDD) in identifying each type of emotion (SMD = −0.24; p-value = 0.014), but these differences were more specific for sad emotional stimuli (SMD = −0.31; p-value = 0.009). No significant differences were observed when BD was compared with children and adolescents diagnosed with attention-deficit/hyperactivity disorder. FER emerges as a potential integrative instrument for guiding diagnosis by enabling discrimination between BD and SCZ or MDD. Enhancing the standardization of adopted tasks could further enhance the accuracy of this tool, leveraging FER potential as a therapeutic target.

* Corresponding author at: Bipolar and Depressive Disorders Unit, Institute of Neuroscience, IDIBAPS CIBERSAM, Hospital Clinic, University of Barcelona, 170 Villarroel St 12-0, 08036 Barcelona, Catalonia, Spain.

E-mail addresses: mdeprisco@clinic.cat (M. De Prisco), violiva@recerca.clinic.cat (V. Oliva), gfico@recerca.clinic.cat (G. Fico), lmontejo@recerca.clinic.cat (L. Montejo), chiara.possidente@studio.unibo.it (C. Possidente), bracco@clinic.cat (L. Bracco), lfortea@recerca.clinic.cat (L. Fortea), anmella@clinic.cat (G. Anmella), dahidalg@clinic.cat (D. Hidalgo-Mazzei), dott.fornaro@gmail.com (M. Fornaro), adebarto@unina.it (A. de Bartolomeis), alessandro.serretti@unibo.it (A. Serretti), amurru@clinic.cat (A. Murru), evieta@clinic.cat (E. Vieta), radua@recerca.clinic.cat (J. Radua).

[1] The authors contributed equally.

https://doi.org/10.1016/j.pnpbp.2023.110847
Received 14 June 2023; Received in revised form 1 August 2023; Accepted 22 August 2023
Available online 23 August 2023

1. Introduction

Cognition involves all the mental processes and skills related to knowledge and awareness. It can be divided into emotion-independent cognition (i.e., cold cognition), which includes attention, memory, processing speed, or executive functions, among other cognitive domains, and emotion-laden cognition (i.e., hot cognition) (Roiser and Sahakian, 2013), also called affective cognition (AC). AC represents an interface where emotional and cognitive processes are integrated to produce behavioral responses (Elliott et al., 2011). Its adequacy seems to be vital for many social and community-based activities (Lopes et al., 2005; Sagliano et al., 2022; Schutte et al., 2001) and can be divided into multiple mutually related domains (e.g., emotion intelligence, implicit or explicit emotion regulation, emotional decision making, reward and punishment processing) (Miskowiak et al., 2019). Among these domains, facial emotion (or expression) recognition (FER) aims at identifying and discriminating specific types of emotions in other individuals. Facial expressions share some core characteristics recognizable across cultural contexts (Elfenbein and Ambady, 2002), and are generally operationalized into six basic and discrete positive (i.e., happiness and surprise), and negative (i.e., anger, disgust, fear, and sadness) emotions (Ekman and Friesen, 1971). The ability to recognize and respond to facial emotional stimuli emerges in infancy (Field et al., 1982) and becomes more complex throughout the development (Herba and Phillips, 2004). FER appears fundamental to social interaction and communication, allowing for appropriate cognitive and behavioral adaptations during interpersonal exchanges (Sagliano et al., 2022). Thus, impaired FER may lead to a deterioration of social relationships in populations diagnosed with neuropsychiatric conditions (De la Torre-Luque et al., 2022), which is associated with worse clinical outcomes (Oliva et al., 2021). A recent systematic review and meta-analysis (Xu et al., 2021) explored FER brain activation and connectivity patterns in healthy subjects and found that several brain structures are deeply involved in perceiving facial emotional stimuli. Specifically, the amygdala appears to be consistently activated across specific and dimensional emotional stimuli, although several other regions may play an important part in specific recognition of anger (e.g., left pallidum, right fusiform face area), fear (e.g., left ventral lateral prefrontal cortex, occipital face area), or disgust (e.g., occipital face area). Alterations in the amygdala's volume, function, or connectivity have been described in several psychiatric disorders, such as schizophrenia (SCZ) (Guo et al., 2023), major depressive disorder (MDD) (Roddy et al., 2021), and bipolar disorder (BD) (Rey et al., 2021).

BD is a severe mental illness affecting up to 2.4% of the world's population (Merikangas et al., 2011). It is characterized by changes in emotions, energy, and thoughts associated with a biphasic course of the illness resulting from genetic, epigenetic, and environmental factors (Fico et al., 2022; Lima et al., 2022; Vieta et al., 2018). While alterations in cold cognition are well described in BD (Cullen et al., 2016), impairments in AC are less clear, despite a growing interest to further characterize its clinical and cognitive profile (Van Rheenen et al., 2019). Emotional intelligence, for example, is commonly compromised in BD, and these individuals appear less able to perceive, use, understand, and manage emotions (Varo et al., 2022; Varo et al., 2019). Reward and punishment processing seem affected, as BD patients show impairments in response inhibition, delay of gratification, and decision-making (Jimenez et al., 2018; Ramírez-Martín et al., 2020). Difficulties in emotion regulation have also been described in people with BD. Two previous systematic reviews and meta-analyses comparing BD with both nonclinical (De Prisco et al., 2022) and clinical (De Prisco et al., 2023) populations found that they were more likely to ruminate and engage in risk-taking behaviors compared to healthy controls and patients with MDD. Finally, people diagnosed with BD compared to healthy controls show more trait difficulties in correctly recognizing facial emotional stimuli (Miskowiak et al., 2019). Impairments in FER have been described in other clinical populations too, such as SCZ (Kohler et al., 2010), MDD (Dalili et al., 2015), borderline personality disorder (Mitchell et al., 2014), or ADHD (Romani et al., 2018). Understanding whether and how FER differs between patients with BD and other psychiatric disorders may help to better distinguish disorders with similar clinical presentations, identify specific neurobiological mechanisms involved in these conditions, or tailor treatments to improve emotion recognition and social functioning in general. This seems crucial, as the only review on this topic is currently limited to comparisons with the SCZ alone (whose FER ability appears to be more impaired) and without a subdivision by type of emotion recognized (Bora and Pantelis, 2016), reinforcing the need for a look that is both broader in terms of comparisons and deeper in terms of the dissection of the FER.

The present systematic review and meta-analysis aims to determine whether and to what extent people diagnosed with BD differ from people with other psychiatric diagnoses in terms of FER. This will be explored with respect to the general domain and specific types of emotions to better delineate differences that may later be useful in research, diagnostic, and clinical settings.

2. Material and methods

The present systematic review and meta-analysis was conducted according to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) (Stroup et al., 2000) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). The protocol of this systematic review and meta-analysis was registered on the International Prospective Register of Systematic Reviews (PROSPERO) (https://www.crd.york.ac.uk/PROSPERO/; protocol CRD42023422035). Deviations from the protocol are reported in the Supplementary Materials.

2.1. Search strategy

We systematically searched the PubMed/MEDLINE, Scopus, EMBASE, and PsycINFO databases from inception to April 26, 2023. Search strategies are provided in the Supplementary Materials. The references of each included study, textbooks, and other materials were hand searched to identify potential additional studies not captured by the original search string.

2.2. Eligibility criteria and study outcomes

Original studies providing quantitative data on FER in people diagnosed with BD and compared with clinical groups (individuals with any other psychiatric diagnosis) were eligible for inclusion. We focused of FER tasks on both emotion identification or discrimination. “Identification” refers to the ability to match an emotional stimulus with its corresponding emotion (e.g., the subject is asked to look at an emotional face and label which emotion the face is expressing). In contrast “discrimination” refers to the ability to discriminate whether two presented faces show the same emotion or not. Psychiatric diagnoses had to be made according to the Diagnostic and Statistical Manual for Mental Disorders (DSM) (APA, 1994, 2000, 2013) or the International Classification of Diseases (ICD) (WHO, 2004) diagnostic criteria. No sample size, age, or language restrictions were applied. We considered for inclusion both observational and interventional studies, and only baseline data were collected. Where populations overlapped in multiple studies, we included the largest study with the most representative data relevant to our objectives. We excluded reviews (no original data), case reports and case series (no reliable control group), and studies conducted on animals (population not covered by our criteria).

2.3. Study selection and data extraction

Two authors (MDP and VO) independently reviewed studies of potential interest, and a third author (LM or GF) was consulted when a

consensus could not be reached. Data extraction included (when available): first author, publication year, geographical region and country, study design, diagnostic criteria and (semi)structured interview adopted, setting of the study, age group (i.e., children/adolescents, adults, older adults, or mixed) of included sample, type of task administered, type of facial expression or emotion showed, type of control group (i.e., specific psychiatric diagnosis), number of cases and controls, type of outcome (e.g., accuracy, reaction time, number of errors, score at a particular scale), mean and standard deviation (SD) of the outcome for cases and controls, mean age, % of females, % of people with comorbid physical conditions, mean score at symptoms severity scales, number of episodes, % of people with comorbid psychiatric disorders, and % of patients under psychotropic medication for both cases and controls, duration of illness, age at onset, % of people diagnosed with BD-I, and % of euthymic, depressed, or (hypo)manic patients for cases only. WebPlotDigitizer was used to extract numerical variables from graphs when necessary (https://automeris.io/WebPlotDigitizer/). When information was unavailable, we contacted the authors to request the required data.

2.4. Methodological quality appraisal

Two authors (MDP and VO) independently assessed the risk of bias in included studies, and a third author (LM or GF) resolved disagreements. The Newcastle-Ottawa Scale (NOS) (Stang, 2010) was adopted to grade the quality of observational studies, and the scores obtained at the NOS were converted to "Agency for Healthcare Research and Quality" (AHRQ) standards, as done elsewhere (Fornaro et al., 2022).

2.5. Statistical analyses

We conducted the meta-analyses using a random-effect model (restricted maximum-likelihood estimator) (Harville, 1977) with the R-package "metafor" (Viechtbauer and Viechtbauer, 2015), using RStudio R version 4.1.2 (R Core Team, 2020). We divided the results into three levels. The upper level included those studies providing data on any type of FER (i.e., individual or combined measures of anger, disgust, fear, happiness, sadness, or surprise). The middle level included those studies providing data on recognition of negative (i.e., individual or combined measures of anger, disgust, fear, or sadness), or positive (i.e., individual or combined measures of happiness, or surprise) emotions. The bottom level included those studies providing data on a specific type of emotion (i.e., individual measures of anger, disgust, fear, happiness, sadness, or surprise). Whenever a study only provided data that could be analyzed at a lower level, we used that data to calculate the necessary information and investigate it at higher levels. Specifically: i) we calculated the weighted mean of the scores obtained from the recognition of individual positive or negative facial expressions to obtain middle-level information; ii) we calculated the weighted mean of the scores obtained from the recognition of individual facial expressions (of any type), to obtain upper-level information. Standardized mean differences (SMD) with their confidence intervals (C.I.) were used as effect sizes and represented by Hedge's g. We conducted a leave-one-out sensitivity analysis by excluding one study at a time from the main analysis and a good-quality only sensitivity analysis by including only good-quality studies according to AHRQ standards. Heterogeneity was assessed by using Cochran's Q test (Cochran, 1950), τ^2 and I^2 statistics (Higgins et al., 2019), and was graphically explored by adopting the graphical display of study heterogeneity (GOSH) method (Olkin et al., 2012). For graphic reasons, GOSH plots were only generated when at least five studies were available. Subgroup and meta-regression analyses were conducted when study-level data was available for the upper level, according to a-priori defined dichotomic (i.e., primary or secondary outcome, presence, or absence of morphing) and continuous predictors (i.e., mean age, % of females, % of euthymic, % of BD-I, % of depressed, % of (hypo)manic, % of people with BD taking antipsychotics, antidepressants, or mood stabilizers, symptoms severity scale, age at onset, duration of illness, duration of stimuli presentation, publication year, NOS score). Whenever Cochran's Q test presented a $p < 0.10$, and the I^2 statistic showed a value >50%, the same subgroup and meta-regression analyses were also conducted for middle and bottom levels. Prediction intervals were calculated. Publication bias was explored by visual examining funnel plots and using Egger's test (Egger et al., 1997) when at least ten studies were available.

3. Results

A total of 3238 references were identified from various sources. After duplicate removal, 1518 studies were further screened. Among these, 1426 were excluded at the title/abstract level and 59 after the full-text evaluation. Finally, 33 studies were included in the present systematic review, of which 26 (Addington and Addington, 1998; Almeida et al., 2010; Almeida et al., 2009; Bellack et al., 1996; Bjertrup et al., 2021; Branco et al., 2018; Darke et al., 2021; Derntl et al., 2012; Goghari and Sponheim, 2013; Golkhatmi et al., 2015; Guyer et al., 2007; Hwang et al., 2021; Lahera et al., 2015; Lee et al., 2013; Navarra-Ventura et al., 2021; Priyesh et al., 2022; Quide et al., 2020; Rossell et al., 2014; Rowland et al., 2012; Rubin et al., 2022; Seymour et al., 2013; Thonse et al., 2018; Vaskinn et al., 2007; Vederman et al., 2012; Wynn et al., 2013; Yalcin-Siedentopf et al., 2014) provided enough data to perform a meta-analysis. The PRISMA flowchart is reported in Fig. 1. The studies excluded from this review are presented in the Supplementary Materials.

3.1. Characteristics of included studies

The 33 studies included were published between 1993 and 2022. People diagnosed with BD were compared to people with SCZ in 20 studies, people with MDD in ten studies, people with attention-deficit/hyperactivity disorder (ADHD) in two studies, people with anxiety or anxiety with comorbid depressive disorders in two studies, people with schizoaffective disorder in two studies, and first-degree relatives with psychiatric disorders in one study. Across all studies, the total number of people with BD was 1506 (range = 7–248) compared to 1973 (range = 10–297) people with other mental health diagnoses. Thirty-one studies were cross-sectional, and two were prospective-cohort studies. Twenty-nine studies focused on adult patients, three included children/adolescents, and one considered adults and children/adolescents in its sample.

The mean age of people diagnosed with BD was 35.64 (±9.36) years, with an age at onset of 23.32 (±5.03) years and a duration of illness of 13.14 (±5.06) years, and 59% of the participants were female. Sixteen studies reported information about the type of BD; among these, 88% of the included patients were diagnosed with BD type I. Regarding mood state, 22 studies provided data: 54% of the sample were euthymic, 29% were depressed, 14% were (hypo)manic, and 3% experienced a mixed episode.

A total of 1249 patients with SCZ were included in this review. Their mean age was 38.37 (±6.15) years, and 42% were female. A total of 282 patients with MDD were included in this review. Their mean age was 35.48 (±5.37) years, and 72% were female. A total of 73 people diagnosed with ADHD were included in this review. Their mean age was 13.44 (±1.92) years, and 35% were female.

Additional information on the studies included in the systematic review and meta-analysis is presented in Table 1 and Supplementary Materials. Further information on the FER tasks used by each study is presented in Supplementary Materials.

3.2. Main analyses

The main results of the meta-analyses conducted are displayed in Table 2 and Fig. 2. Among the 26 studies included in the meta-analysis, 17 studies compared people diagnosed with BD to SCZ, six studies compared people diagnosed with BD to MDD, two studies compared BD to ADHD, and one study compared people diagnosed with BD to both

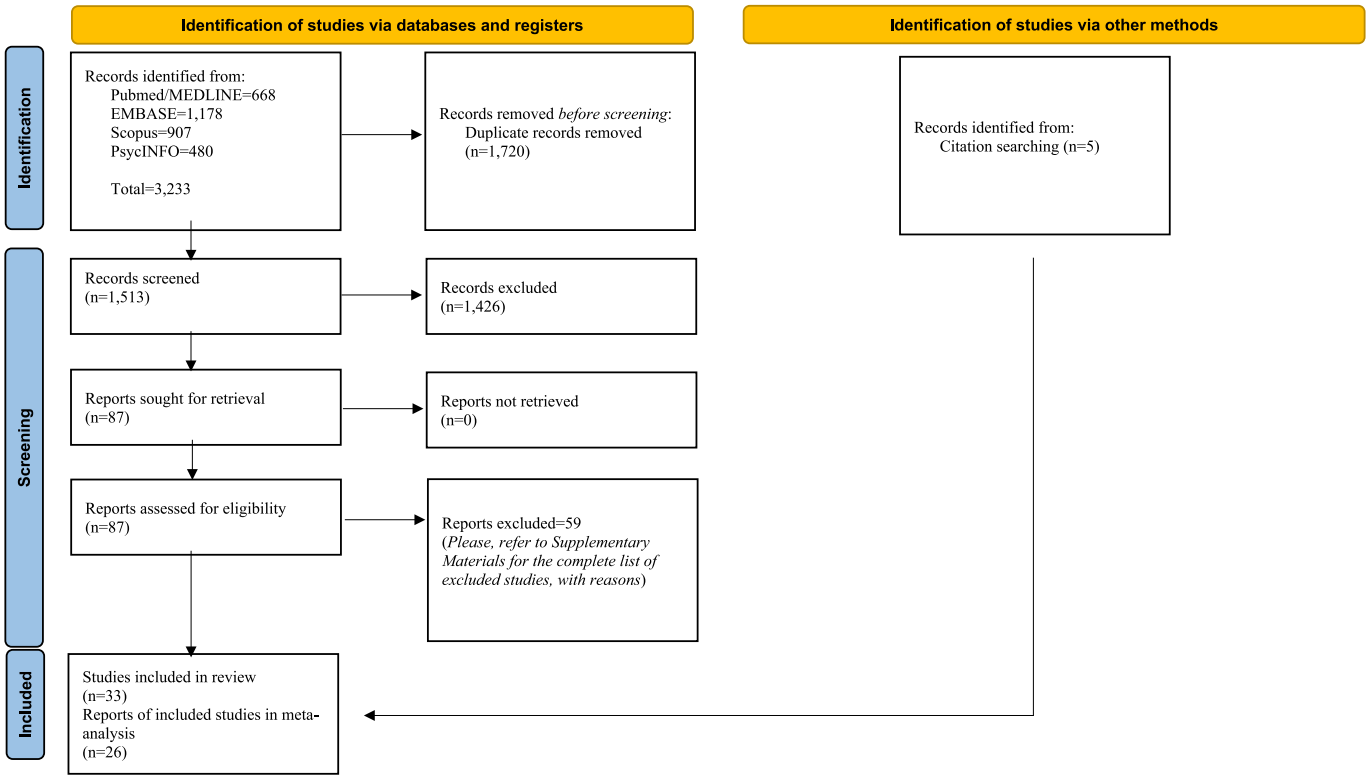


Fig. 1. PRISMA flowchart, 2020 edition, adapted.
From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 Statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/.

SCZ and MDD.

Eighteen studies (Almeida et al., 2010; Almeida et al., 2009; Bjertrup et al., 2021; Branco et al., 2018; Darke et al., 2021; Daros et al., 2014; Derntl et al., 2012; Goghari and Sponheim, 2013; Golkhatmi et al., 2015; Guyer et al., 2007; Lelli-Chiesa et al., 2011; Mourao-Miranda et al., 2012; Rubin et al., 2022; Ruocco et al., 2014; Schaefer et al., 2010; Seymour et al., 2013; Vederman et al., 2012; Yalcin-Siedentopf et al., 2014) provided only bottom-level data from which we calculated middle- and/or upper-level information. Two studies (Lahera et al., 2015; Rowland et al., 2012) provided data on emotion identification using two different tasks; in these cases, we used data from the task more comparable to the others included.

Overall, people with BD were significantly more accurate than people with SCZ when considering any FER during the identification tasks (SMD = 0.27; 95%CI = 0.078, 0.462; *p*-value = 0.006). No differences were found when examining the differences between positive and negative emotion identification. Looking at specific emotion types, people with BD were significantly more accurate than people with SCZ at recognizing angry (SMD = 0.46; 95%CI = 0.27, 0.64; p-value = 1.19e-06), fearful (SMD = 0.38; 95%CI = 0.16, 0.61; p-value = 8.2e-04), and sad (SMD = 0.33; 95%CI = 0.04, 0.62; p-value = 0.026) faces. People with BD were significantly faster at identifying sad faces (SMD = −0.44; 95%CI = −0.662, −0.218; p-value = 1.04e-04).

On the other hand, people diagnosed with BD were significantly less accurate than people with MDD when considering any FER during the identification tasks (SMD = −0.24; 95%CI = −0.43, −0.05; p-value = 0.014). No differences were found when examining the differences between positive and negative emotion identification. When looking at specific emotion types, people with BD were significantly less accurate than people with MDD at recognizing sad faces (SMD = −0.31; 95%CI = −0.54, −0.08; p-value = 0.009).

Finally, no significant differences were observed between BD and ADHD.

Additional details on the main analyses are presented in the Supplementary Materials.

3.3. Meta-regression analyses

We conducted meta-regression analyses to explore the role of dichotomic and continuous predictors on FER.

In studies comparing BD and SCZ: i) increasing BD depression symptom severity scale scores (β = 0.272), or decreasing % of people with BD taking antipsychotics (β = −1.335) significantly predicted higher accuracy scores in identifying negative emotions; ii) decreasing NOS score (β = −0.551) significantly predicted higher reaction time in identifying positive emotions; iii) decreasing % of females among people with BD (β = −5.02) significantly predicted higher accuracy scores in identifying disgust.

In studies comparing BD and MDD: i) increasing publication year (β = 0.13), decreasing BD depression symptom severity scale scores (β = −0.526), and the use of a morphed FER task (β = 1.094) significantly predicted higher accuracy scores in identifying positive emotions; ii) increasing % of people in (hypo)mania among people with BD (β = 1.006), and decreasing NOS scores (β = −0.272) significantly predicted higher accuracy scores in identifying disgust.

Additional details on the meta-regression analyses are presented in the Supplementary Materials.

3.4. Sensitivity analyses

It was not possible to conduct a good-quality studies only sensitivity analysis for any comparisons. To further assess outliers and heterogeneity, the GOSH plots were graphically inspected.

In studies comparing BD and SCZ: i) by removing (Derntl et al., 2012) from the comparison assessing reaction time to identify each type of emotion, the overall effect size became significant with no heterogeneity

Table 1
Characteristics of the studies included in the systematic review and meta-analysis.

Author, year, country	Study design	Population (n)	Mood state patients with BD (%)	Mean age	Percentage of females	Primary outcome of the study	Diagnostic criteria	Instrument adopted	Emotion type	Outcome type	Quality of the study (NOS/)
(Addington and Addington, 1998), Canada	Prospective	BD (40) SCZ (40)	Euthymic: 97.5 Depressed: 2.5	38.5 ± 11 NA	75% 32.5%	To test the hypothesis that deficits in facial recognition are a stable trait.	DSM-III-R (SCID)	POFA	Anger, disgust, fear, happiness, sadness, surprise	Identification (total score); discrimination (total score)	6 (POOR)
(Almeida et al., 2009), USA	Cross-sectional	BD (15 BD-I) MDD (16)	Depressed: 100	36.6 ± 11.9 32.3 ± 36.6	50% 81.2%	To examine amygdala-prefrontal connectivity in BD and MDD depressed patients during happy and sad emotion processing.	DSM-IV (SCID)	POFA	Happiness, sadness	Identification (accuracy)	5 (FAIR)
(Almeida et al., 2010), USA	Cross-sectional	BD (30 BD-I) MDD (15)	Euthymic: 50 Depressed: 50	34.92 ± 9.85 32.74 ± 9.87	80% 86.7%	To examine whether abnormally heightened amygdala activity in response to emotional facial expressions was a persistent marker of BD during remission and depression, a state marker of depression in both BD and recurrent MDD, or a specific marker of depression in either BD or recurrent MDD.	DSM-IV (SCID-P)	POFA	Fear, happiness, sadness	Identification (accuracy)	6 (FAIR)
(Bellack et al., 1996), USA	Cross-sectional	BD (11) SCZ/SCA (35)	NA	39.27 ± 5.75 39.11 ± 9.33	64% 51.4%	To assess the ability to discriminate affect states and determine the intensity of them in a sample of SCZ/SCA patients compared to BD subjects and HCs	DSM-III-R (SCID-P)	POFA, FOE	Anger, disgust, fear, happiness, sadness, surprise	Identification (total score); discrimination (total score)	4 (POOR)
(Bjertrup et al., 2021), Denmark	Prospective	BD (30) MDD (22)	Euthymic: 100	29.4 ± 4.2 32.3 ± 5.1	100% 100%	To investigate emotion processing in pregnant MDD and BD women in full or partial remission and in healthy pregnant women in comparison with non-pregnant age matched women.	DSM-IV (MINI)	POFA	Anger, disgust, fear, happiness, sadness, surprise	Identification (accuracy)	7 (POOR)
(Branco et al., 2018), Brazil	Cross-sectional	BD (17 BD-I, 13 BD-II) MDD (18)	Euthymic: 33 Depressed: 67	42.9 ± 13.12 32 ± 12.33	80% 72%	To study the accuracy in identifying facial expressions and the perceived intensity of them in patients with MDD and BD, as compared to HCs.	DSM-V	NA	Anger, disgust, fear, happiness, sadness, surprise	Identification (number of correct)	6 (POOR)
(Darke et al., 2021), Australia	Cross-sectional	BD (15) SCZ spectrum (36)	Euthymic: 0 (Hypo) manic: NA Depressed: NA Mixed: NA	36.6 ± 14.8 34.44 ± 9.44	40% 35%	To assess face processing deficits in inpatients with a range of psychiatric diagnosis and HCs.	DSM-IV	MIMI, FEED	Disgust, fear	Identification (accuracy); discrimination (accuracy)	3 (POOR)
(Daros et al., 2014), Canada	Prospective	BD (16 BD-I) SCZ (24)	(Hypo) manic: 31 Depressed: 50 Mixed: 19	26.63 ± 6.27 22.58 ± 5.69	44% 35%	To compare facial emotion recognition deficits in psychotic BD and SCZ during an acute phase of illness.	DSM-IV	PEAT	Happiness, sadness	Identification (accuracy)	6 (FAIR)
(Derntl et al., 2012), Germany	Cross-sectional	BD (24) SCZ (24) MDD (24)	NA	44 ± 9.8 40.1 ± 8.7	50% 50% 50%	To compare performance regarding three different core components of empathy in patients suffering from SCZ, BD and MDD.	DSM-IV	3D Facial Expression Task	Anger, disgust, fear, happiness, neutral, sadness	Identification (accuracy, reaction time)	6 (FAIR)

(*continued on next page*)

Table 1 (*continued*)

Author, year, country	Study design	Population (n)	Mood state patients with BD (%)	Mean age	Percentage of females	Primary outcome of the study	Diagnostic criteria	Instrument adopted	Emotion type	Outcome type	Quality of the study (NOS/)
				41.1 ± 10.6							
(Goghari and Sponheim, 2013), USA	Cross-sectional	BD (16 BD-I) SCZ (27)	NA	46.2 ± 11.3 38.9 ± 12.3	81% 70%	To determine the pattern of facial emotion recognition impairments in stable SCZ patients, BD, and healthy controls.	DSM-IV-TR	Pennsylvania emotive faces	Anger, fear, happy, neutral, sad	Identification (accuracy, reaction time)	4 (POOR)
(Golkhatmi et al., 2015), Iran	Cross-sectional	BD (30) MDD (30)	(Hypo) manic: 100	29.13 ± 8.08 40.2 ± 12.65	53% 60%	To compare facial emotion recognition among MDD, BD during a manic phase and HCs.	DSM-V	POFA	Anger, disgust, fear, happiness, sadness, surprise	Identification (total score)	3 (POOR)
(Guyer et al., 2007), USA	Cross-sectional	BD (42 BD-I) SMD (39) ADHD/CD (35) ANX/MDD (44)	NA	12.8 ± 2.5 11.8 ± 2.1 14.8 ± 1.6 13.1 ± 2.5	48% 28,2% 28,6% 47.7%	To investigate the difference among BD, SMD, ANX/MDD, and ADHD/CD patients' performance on face-emotion labeling task.	DSM-IV (K-SADS-PL)	DANVA	Anger, fear, happiness, sadness	Identification (number of errors)	6 (FAIR)
(Hwang et al., 2021), Republic of Korea	Cross-sectional	BD (53) SCZ (52)	NA	27 ± 6,8 26.4 ± 6.9	51% 48%	To compare the emotional perception ability and the functional connectivity within the fronto–temporal–occipital circuit in BD and SCZ.	DSM-V	NA	Pleasant, unpleasant	Discrimination (correction rate)	4 (POOR)
(Lahera et al., 2015), Spain	Cross-sectional	BD (46) SCZ (49)	Euthymic: 100	38.6 ± 10.63 40.4 ± 10.5	63% 43%	To compare the profile of attributional style of a group of outpatients with BD and SCZ, and a group of healthy controls – along with other social cognition domains – such as emotion recognition and ToM.	DSM-IV-TR	ER-40, FEIT, FEDT	Anger, disgust, happiness, sadness, shame, surprise	Identification (total score); discrimination (total score)	3 (POOR)
(Lee et al., 2013), USA	Cross-sectional	BD (46 BD-I, 22 BD-II) SCZ (38)	Euthymic: 76 (Hypo) manic: NA Depressed: NA Mixed: NA	43.9 ± 10.6 44.7 ± 9.1	NA NA	To compare the level and pattern of social and nonsocial cognitive performance in BD and SCZ patients using behavioral tasks.	DSM-IV (SCID)	SETT, METT	Anger, disgust, fear, happiness, sadness, surprise	Identification (accuracy)	7 (GOOD)
(Lelli-Chiesa et al., 2011), UK	Cross-sectional	BD (40 BD-I) PsyRs (17)	Euthymic: 100	44 ± 11.9 32.5 ± 11.4	52.5% 63.6%	To examine the potential influence of the COMT Val158Met polymorphism may contribute on the phenotypic variation in clinical diagnosis using sad facial affect processing as a probe for its neural action.	DSM-IV (SCID)	POFA	Sadness	Identification (accuracy, reaction time)	6 (FAIR)
(McClure et al., 2003), USA	Cross-sectional	BD (11) ANX (10)	NA	13.78 ± 1.68 13.78 ± 1.68	18% 50%	To compare facial expression recognition in adolescents with mood and anxiety disorders.	DSM-IV (K-SADS-PL)	NA	Anger, fear, happiness, sadness	Identification (number of errors)	4 (POOR)

(*continued on next page*)

Table 1 (*continued*)

Author, year, country	Study design	Population (n)	Mood state patients with BD (%)	Mean age	Percentage of females	Primary outcome of the study	Diagnostic criteria	Instrument adopted	Emotion type	Outcome type	Quality of the study (NOS/)
(Mourao-Miranda et al., 2012), UK	Cross-sectional	BD (18) MDD (18)	NA	36 ± 11 32 ± 9	78% 95%	To compare the patterns of neural activity elicited by happy and neutral facial stimuli in BD and MDD.	DSM-IV-TR (SCID-P)	POFA	Happiness	Identification (GPC accuracy)	6 (FAIR)
(Navarra-Ventura et al., 2021), Spain	Cross-sectional	BD (46 BD-I, 14 BD-II) SCZ/SCZA (60)	Euthymic: 100	47.2 ± 8.75 44.9 ± 8.8	50% 50%	To compare emotion recognition, affective ToM, and first- and second-order cognitive ToM in BD, SCZ and HCs.	DSM-IV-TR	POFA	Anger, disgust, fear, happiness, sadness, surprise	Identification (total score)	6 (FAIR)
(Priyesh et al., 2022), India	Cross-sectional	BD (26) SCZ (24)	Euthymic: 100	36.6 ± 69.5 39.5 ± 9.4	50% 50%	To compare facial emotion recognition deficits in BD, SCZ and HCs.	DSM-V	TRENDS	Anger, fear, happiness	Identification (accuracy, reaction time)	4 (POOR)
(Quide et al., 2020), Australia	Cross-sectional	BD (65 BD-I) SCZ (60)	NA	35.85 ± 12.14 41.16 ± 11.05	71% 40%	To determine the relationship between structural brain alterations and social cognitive deficits in patients diagnosed with SZ or BD.	ICD-10 (DIP)	TASIT	Anger, disgust, fear, happiness, sadness, surprise	Identification (total score)	5 (POOR)
(Rossell et al., 2014)	Cross-sectional	BD (43) SCZ (54)	Euthymic: 25 Depressed: 75	40.5 ± 10.64 42.17 ± 10.5	63% 35%	To examine facial affect processing in two different groups of psychosis patients and a group of healthy controls.	DSM-IV	NA	Anger, disgust, fear, happiness, neutral, sadness, surprise	Identification (accuracy, reaction time); discrimination (accuracy, reaction time)	5 (POOR)
(Rowland et al., 2012), Australia	Cross-sectional	BD (33 BD-I) SCZ (56)	Euthymic: 36 (Hypo) manic: 36 Depressed: 3 Mixed: 25	40.67 ± 11.27 44.57 ± 10.37	45% 43%	To compare the ability in emotion recognition in patients with BD and SCZ, and in HCs	DSM-IV	TASIT / POFA, FEEST	Anger, disgust, fear, happiness, sadness, surprise	Identification (total score / accuracy)	3 (POOR)
(Rubin et al., 2022), USA	Cross-sectional	BD (113) SCZA (163) SCZ (181)	Euthymic: 0 (Hypo) manic: NA Depressed: NA Mixed: NA	38.1 ± 11.6 40.4 ± 10.8 41.1 ± 11.4	55% 56% 46%	To compare facial emotion recognition in BD, SCZA and SCZ and HCs.	DSM-IV (SCID-I)	Cohn-Kanade, DARE	Anger, disgust, fear, happiness, sadness, surprise	Identification (accuracy, reaction time)	5 (POOR)
(Ruihua et al., 2021), China	Cross-sectional	BD (30) MDD (30)	Euthymic: 0 (Hypo) manic: NA Depressed: NA Mixed: NA	24.25 ± 9.03 28.3 ± 9.73	56% 63%	To compare facial emotion recognition in BD and MDD	DSM-IV	POFA	Anger, disgust, fear, happiness, sadness, surprise	Identification (accuracy)	6 (FAIR)
(Ruocco et al., 2014), USA	Cross-sectional	BD (248) SCZA (130)	Euthymic: 0 (Hypo) manic: NA	36.22 ± 12.72	63% 41%	To compare emotion recognition deficits in SCZ, SCZA and BD with psychosis, to determine the familiarity of emotion recognition deficits across	DSM-IV (SCID-I)	ER-40	Anger, fear, happiness, sadness	Identification (accuracy, reaction time)	5 (POOR)

(*continued on next page*)

Table 1 (*continued*)

Author, year, country	Study design	Population (n)	Mood state patients with BD (%)	Mean age	Percentage of females	Primary outcome of the study	Diagnostic criteria	Instrument adopted	Emotion type	Outcome type	Quality of the study (NOS/)
		SCZ (297)	Depressed: NA Mixed: NA	37.28 ± 11.79 35.79 ± 12.72	32%	these disorders, and to evaluate emotion recognition deficits in non-psychotic relatives with and without elevated Cluster A and Cluster B personality disorder traits.					
(Schaefer et al., 2010), USA	Cross-sectional	BD (9 BD-I, 21 BD-II) MDD (31)	Depressed: 100	46.8 ± 11.8 45 ± 12.8	62% 44%	To compare the accuracy and sensitivity of emotion perception between BD, MDD and HCs.	DSM-IV (SCID-P)	POFA	Anger, disgust, fear, happiness, sadness, surprise	Identification (accuracy)	4 (POOR)
(Seymour et al., 2013), USA	Cross-sectional	BD (27 BD-I, 3 BD-II) ADHD (38)	Euthymic: 70 (Hypo) manic: 13 Depressed: 10 Mixed: 7	13.03 ± 2.99 12.08 ± 2.78	33% 42%	To compare emotional face identification ability among youths with BD, ADHD, or TDCs.	DSM-IV (K-SADS-PL)	DANVA	Anger, fear, happiness, sadness	Identification (number of errors)	4 (POOR)
(Thonse et al., 2018), India	Cross-sectional	BD (71) SCZ (91)	Euthymic: 100	38.1 ± 10.1 36.32 ± 9.25	48% 35%	To compare the facial emotion recognition abilities and socio-occupational functioning in SCZ and BD.	DSM-IV-TR (MINI-plus)	TRENDS	Anger, fear, happiness, sadness	Identification (total score)	6 (POOR)
(Vaskinn et al., 2007)	Cross-sectional	BD (21) SCZ (31)	Euthymic: 100	38.1 ± 9.3 31.3 ± 9.5	48% 35%	To investigate visual and auditory emotion perception in schizophrenia and bipolar disorder.	DSM-IV	POFA	Anger, fear, happiness, sadness, surprise, shame	Identification (total score); discrimination (total score)	5 (POOR)
(Vederman et al., 2012), USA	Cross-sectional	BD (119) MDD (78)	NA	37 ± 11.8 38.9 ± 12.5	67% 69%	To compare perceptual accuracy in affect identification in visual and auditory domains among BD, MDD and HCs.	DSM-IV (SCID-I; DIGS)	FEPT	Anger, fear, happiness, sadness	Identification (accuracy)	4 (POOR)
(Wynn et al., 2013), USA	Cross-sectional	BD (57) SCZ (30)	Euthymic: 100	44.9 ± 10.4 45.3 ± 9.4	43% 35%	To compare the ERP N170 and N250 during facial affect processing in BD, SCZ, and HCs.	DSM-IV (SCID-I)	POFA	Anger, fear, happiness, sadness, shame, surprise	Identification (accuracy)	5 (POOR)
(Yalcin-Siedentopf et al., 2014), Austria	Cross-sectional	BD (57) SCZ (40)	Euthymic: 100	41.9 ± 11.7 40.3 ± 8.5	65% 45%	To compare the performance on a FAR task in BD remitted, SCZ remitted and HCs.	DSM-IV (MINI)	FEEL	Anger, disgust, fear, happiness, sadness, surprise	Identification (accuracy)	6 (FAIR)

Notes: ADHD - Attention Deficit-Hyperactivity disorder; **ANX** - Anxious Disorders; **BD** - Bipolar Disorder; **BD-I** - Bipolar Disorder Type 1; **BD-II** - Bipolar Disorder Type II; **BPD** - Borderline Personality Disorder; **CD** - Conduct Disorder; **Cohn-Kanade** - Cohn-Kanade Action Unit-Coded Facial Expression Database; **COMT** - Catechol-O-methyltransferase; **DANVA** - Diagnostic Analysis of Non-Verbal Accuracy; **DARE** - Dynamic Affect Recognition Evaluation Task; **DIGS** - Diagnostic Interview for Genetic Studies; **DIP** - The Diagnostic Interview for Psychoses; **DSM-III-R** - Diagnostic and Statistical Manual of Mental Disorders – third ed. revised; **DSM-IV** - Diagnostic and Statistical Manual of Mental Disorders – fourth ed.; **DSM-IV-TR** - Diagnostic and Statistical Manual of Mental Disorders – fourth ed. – Text Revision; **DSM-V** - Diagnostic and Statistical Manual of Mental Disorders – fifth ed.; **ER-40** - Penn Emotion Recognition-40; **ERP**- Event Related Potential; **FAR** - Facial Affect Recognition; **FEDT** - Facial Emotion Discrimination Test; **FEED** - Facial Expression and Emotions Database; **FEEL** - Facial Expression Emotion Labeling; **FEEL** - Facially Expressed Emotion Labeling; **FEEST** - Facial Expressions of Emotion: Stimuli and Tests; **FEIT** - Facial Emotion and Identification Test; **FEPT** - Facial Emotion Perception Test; **FOE** - The Face of Emotions; **HCs** - Healthy Controls; **IAPS** - International Affective Picture System; **ICD-10** - International Classification of Diseases; **K-SADS-PL** - Kiddie Schedule for Affective Disorders and Schizophrenia, present and lifetime version; **MDD** - Major Depressive Disorder; **METT** - Micro-expression Training Tool; **MIMI** - MIMI Facial Expression Database; **MINI** - The Mini-International Neuropsychiatric Interview; **NA** - Not available; **NOS** - Newcastle-Ottawa Scale; **PEAT** - Penn Emotion Acuity Test; **POFA** - Pictures of Facial Affect; **PsyRs** – relatives with a different psychiatric diagnosis (other than BD); **RCT** - Randomized Clinical Trial; **RoB 2** - Cochrane risk-of-bias tool for randomized trials, version 2; **SCAN** - Schedules for Clinical Assessment in Neuropsychiatry; **SCID** - Structured Clinical Interview for DSM Disorders; **SCID-P** -Structured Clinical Interview for DSM Disorders-Patient version; **SCZ** - Schizophrenia; **SETT** - Subtle Expression Training Tool; **SMD** - Severe Mood Dysregulation; **TASIT** - The Awareness of Social Inference Test; **TDC** - Typically Developed Control; **ToM** - Theory of Mind; **TRENDS** - Tool for Recognition of Emotions in Neuropsychiatric Disorders.

(SMD = −0.219; 95%CI = −0.402, −0.037; *p*-value = 0.019); ii) by removing (Bellack et al., 1996) from the comparison assessing accuracy to discriminate each type of emotion, the overall effect size became significant (SMD = 0.51; 95%CI = 0.014, 1.005; *p*-value = 0.044); iii) by removing (Goghari and Sponheim, 2013) from the comparison assessing reaction time to identify negative emotions, the overall effect size became significant (SMD = −0.229; 95%CI = −0.446, −0.012; p-value = 0.038); iv) by removing (Yalcin-Siedentopf et al., 2014) from the comparison assessing reaction time to identify disgust, the overall effect size became significant (SMD = 0.237; 95%CI = 0.019, 0.454; p-value = 0.033); v) by removing (Rubin et al., 2022) from the comparison assessing reaction time to identify fear, the overall effect size became not significant; vi) by removing (Yalcin-Siedentopf et al., 2014) from the comparison assessing reaction time to identify happiness, the overall effect size became significant (SMD = 0.283; 95%CI = 0.077, 0.489; p-value = 0.007); vii) by removing any one among (Goghari and Sponheim, 2013; Rubin et al., 2022) from the comparison assessing reaction time to identify sadness, the overall effect size became not significant.

In studies comparing BD and MDD: i) by removing (Vederman et al., 2012) from the comparison assessing accuracy to identify any emotion, the overall effect size became not significant; ii) by removing (Golkhatmi et al., 2015) from the comparison assessing accuracy to identify sad faces, the overall effect size became not significant.

Additional details on the sensitivity analyses and the GOSH plots are presented in the Supplementary Materials.

3.5. Publication bias

Publication bias was not observed for the only comparison where at least ten studies were available (overall FER accuracy between BD and SCZ). The Egger test was not significant (z = −0.5; p-value = 0.6).

Additional details on the publication bias are presented in the Supplementary Materials.

3.6. Characteristics of the studies and comparisons included in the qualitative synthesis

Seven studies (Daros et al., 2014; Lelli-Chiesa et al., 2011; McClure et al., 2003; Mourao-Miranda et al., 2012; Ruihua et al., 2021; Ruocco et al., 2014; Schaefer et al., 2010) were included in the systematic review only. In one study (Lelli-Chiesa et al., 2011), the control group included first-degree relatives diagnosed with psychiatric disorders without providing data stratified by individual diagnoses. In one study (McClure et al., 2003), the control group included people diagnosed with anxiety disorders. Still, no other study provided data on this comparison, and a meta-analysis was not possible. In one study (Ruihua et al., 2021) the selected FER task was not comparable to the others regarding the paradigm used. One study (Ruocco et al., 2014) did not report data on direct comparisons between BD and control groups. Three studies (Daros et al., 2014; Mourao-Miranda et al., 2012; Schaefer et al., 2010) did not report the SD, and because we did not want to further increase the expected heterogeneity, we decided not to use any method to estimate it from the available data.

Two studies did not find significant differences in FER between people diagnosed with BD and those with MDD (Schaefer et al., 2010) or first-degree relatives diagnosed with other psychiatric disorders (Lelli-Chiesa et al., 2011). In one study (Ruocco et al., 2014) comparing BD and SCZ, individuals with SCZ showed poorer FER performance, while in another study (Daros et al., 2014), individuals diagnosed with BD and SCZ were less accurate in recognizing sad and happy or mostly sad facial expressions, respectively, compared to healthy controls. People with BD committed more errors during a FER task when compared with people with anxiety disorders in one study (McClure et al., 2003). One study (Mourao-Miranda et al., 2012) comparing BD and MDD found a significantly higher predictive probability for intense happy face recognition in the latter. Finally, one study found better recognition of anger and

Table 2
Results of the meta-analyses in detail.

Control, diagnosis	Emotion type	Outcome	Studies, n	BD patients, n	Control, n	SMD	95% CI	p-value	95% PI	I^2 (%)	tau^2	Q-test p-value
Identification												
Upper level – any facial emotion												
SCZ	Any	Accuracy	17	766	876	**0.27**	**0.078, 0.462**	**0.006**	−0.405, 0.946	70.6	0.109	<0.001
		Reaction time	5	222	310	0.574	−0.799, 1.947	0.412	−2.738, 3.887	97.7	2.366	<0.001
MDD	Any	Accuracy	7	255	203	**−0.236**	**−0.425, −0.047**	**0.014**	**−0.425, −0.047**	0	0	0.378
ADHD	Any	Errors	2	72	73	1.907	−1.932, 5.747	0.33	−4.712, 8.527	98.6	7.57	<0.001
Middle level – positive/negative facial emotions												
SCZ	Positive	Accuracy	6	269	352	0.1	−0.061, 0.261	0.224	−0.061, 0.261	0	0	0.345
		Reaction time	3	155	232	−0.07	−0.494, 0.354	0.746	−0.784, 0.644	61.1	0.086	0.068
	Negative	Accuracy	7	284	388	0.18	−0.077, 0.437	0.17	−0.37, 0.73	54.6	0.062	0.045
		Reaction time	3	155	232	−0.189	−0.394, 0.016	0.07	−0.394, 0.016	0	0	0.517
MDD	Positive	Accuracy	6	225	185	−0.071	−0.317, 0.175	0.57	−0.448, 0.305	22.2	0.021	0.09
	Negative	Accuracy	7	255	203	−0.117	−0.308, 0.0724	0.225	−0.312, 0.077	0.6	0.001	0.333
ADHD	Positive	Errors	2	72	73	1.242	−0.38, 2.865	0.133	−1.52, 4.005	94.8	1.301	<0.001
	Negative	Errors	2	72	73	2.143	−1.99, 6.276	0.309	−4.984, 9.27	98.7	8.778	<0.001
Lower level – specific facial emotions												
SCZ	Anger	Accuracy	4	210	272	**0.458**	**0.273, 0.643**	**1.19e-06**	**0.273, 0.643**	0	0	0.884
		Reaction time	2	129	208	−0.059	−0.278, 0.161	0.601	−0.278, 0.1611	0	0	0.486
	Disgust	Accuracy	3	194	245	0.069	−0.323, 0.462	0.729	−0.608, 0.747	67.3	0.079	0.049
	Fear	Accuracy	4	210	272	**0.384**	**0.159, 0.608**	**8.20e-04**	−0.077, 0.69	19.8	0.011	0.441
		Reaction time	2	129	208	−0.076	−0.593, 0.441	0.774	−0.868, 0.717	62	0.094	0.104
	Happiness	Accuracy	4	210	272	0.155	−0.118, 0.429	0.267	−0.288, 0.598	40.9	0.032	0.172
		Reaction time	2	129	208	−0.099	−0.753, 0.554	0.766	−1.144, 0.945	75	0.173	0.045
	Sadness	Accuracy	4	210	272	**0.331**	**0.038, 0.623**	**0.026**	−0.161, 0.823	46.9	0.04	0.13
		Reaction time	2	129	208	**−0.44**	**−0.662, −0.218**	**1.04e-04**	**−0.662, −0.218**	0	0	0.4
	Surprise	Accuracy	2	170	221	0.037	−0.166, 0.24	0.722	−0.166, 0.024	0	0	0.434
MDD	Anger	Accuracy	5	210	172	−0.046	−0.252, 0.161	0.664	−0.252, 0.161	0	0	0.212
	Disgust	Accuracy	4	91	94	0.039	−0.459, 0.537	0.878	−0.883, 0.962	61.8	0.157	0.047
	Fear	Accuracy	5	210	169	−0.13	−0.382, 0.123	0.315	−0.494, 0.235	20.8	0.018	0.287
	Happiness	Accuracy	5	218	163	−0.106	−0.312, 0.099	0.309	−0.312, 0.099	0	0	0.432
	Sadness	Accuracy	7	255	203	**−0.309**	**−0.541, −0.076**	**0.009**	−0.683, 0.066	23	0.022	0.377
	Surprise	Accuracy	2	37	52	−0.525	−1.18, 0.129	0.116	−1.44, 0.389	43.9	0.106	0.182
	Neutral	Accuracy	3	69	55	0.091	−0.27, 0.452	0.622	−0.27, 0.452	0	0	0.421
ADHD	Anger	Errors	2	72	73	1.678	−1.469, 4.824	0.296	−3.74, 7.096	98.2	5.064	<0.001
	Fear	Errors	2	72	73	1.936	−2.579, 6.452	0.401	−5.857, 9.73	98.9	10.5	<0.001
	Happiness	Errors	2	72	73	1.242	−0.38, 2.865	0.133	−1.52, 4.005	94.8	1.301	<0.001
	Sadness	Errors	2	72	73	2.88	−1.99, 7.756	0.247	−5.531, 11.292	98.8	12.228	<0.001
Discrimination												
Upper level – any facial emotion												
SCZ	Any	Accuracy	7	229	297	0.442	−0.007, 0.891	0.054	−0.722, 1.606	83.1	0.3	<0.001

Notes: BD – Bipolar Disorder; CI – Confidence Intervals; MDD – Major Depressive Disorder; PI – Prediction Intervals; SCZ – Schizophrenia.

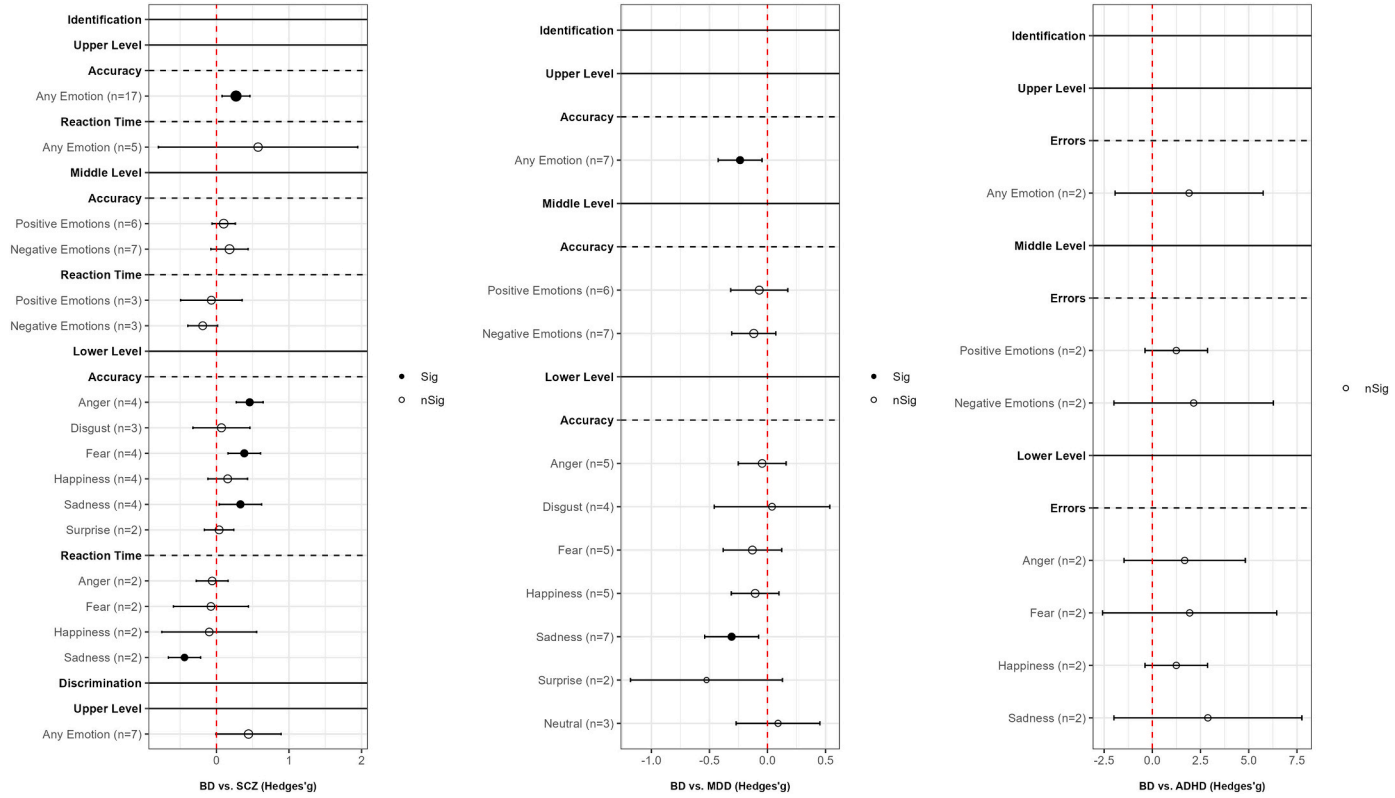


Fig. 2. Differences in facial emotion identification or discrimination between people with bipolar disorder and people with schizophrenia spectrum disorder (left), major depressive disorder (center), and attention deficit/hyperactivity disorder (right). Overall results of the comparisons included in the meta-analysis. Legend: *ADHD*, Attention Deficit/Hyperactivity Disorder; *BD*, Bipolar Disorder; *MDD*, Major Depressive Disorder; *SCZ*, Schizophrenia spectrum disorder. Point size is proportional to the number of patients included in that specific comparison.

sadness than happiness in people diagnosed with MDD compared to BD.

Additional details on these studies are presented in Table 1 and Supplementary Materials.

4. Discussion

The present systematic review and meta-analysis aimed to assess the differences in FER between people diagnosed with BD and other clinical populations. Overall, people with BD were more accurate than people diagnosed with SCZ at identifying any type of emotional faces at the FER task, with the highest accuracy for angry, fearful, or sad faces. On the other hand, they were less accurate than people diagnosed with MDD at identifying both emotional faces in general and sad emotional stimuli. No significant differences were observed between BD and ADHD.

Difficulties in FER have largely been described and studied in individuals diagnosed with SCZ (Fusar-Poli et al., 2022b; Green et al., 2019; Maat et al., 2015), and these issues have also been observed, albeit to a lesser extent, in their first-degree relatives (Fusar-Poli et al., 2022a). Our results on AC indicating a greater impairment of SCZ compared to BD are consistent with meta-analytic evidence on cold cognition, in which the former performed worse than the latter in terms of verbal fluency, working memory, and executive control (Bortolato et al., 2015). The observed impairments in AC may also be influenced by alterations in visual perception processing. Indeed several structural or functional abnormalities have been found in SCZ, both in cortical and non-cortical areas of visual perception (Adámek et al., 2022). People diagnosed with BD too have potential alterations in visual perception processing, although to a lesser extent than described in SCZ. Compared to the latter, the former show greater cortical thickness of visual brain areas (Reavis et al., 2017) or specific differences in the electroretinography (Hébert et al., 2020).

When considering specific types of FER, people with BD identified threat-related expressions (i.e., anger and fear) better compared with people with SCZ. The amygdala and the extended amygdala (including part of the subaccumbens) are involved in recognizing and processing these kinds of emotional stimuli and orchestrating a range of behaviors that fall under the fight-or-flight response (Šimić et al., 2021), so the differences we observed could be at least in part related to variations in the functioning of this structure. Indeed, individuals diagnosed with SCZ show reduced left and right amygdala volumes, in addition to a more stable pattern of diminished connectivity with the prefrontal cortex compared to BD, where more heterogeneous findings are described (Ho et al., 2019) in line with studies focusing on AC in general (de Siqueira et al., 2023). Another factor that may partially explain the greater propensity of individuals with BD to identify angry or fearful faces accurately is a history of childhood maltreatment, which appears to be highly prevalent in this population (Agnew-Blais and Danese, 2016). It seems that individuals exposed to childhood maltreatment (e.g., physical abuse) are more likely to recognize negative emotional stimuli (Pollak and Sinha, 2002), suggesting that FER may be mediated by learning (Pollak et al., 2009). Although this perspective seems interesting, it remains speculative because the few studies that have related FER and childhood maltreatment in BD have not found significant associations (Fares-Otero et al., 2023), and high rates of childhood trauma have also been described in SCZ (Matheson et al., 2013), so further studies comparing the two populations on this particular aspect are needed to confirm or reject these hypotheses. Finally, it is important to consider how the type of stimulus used may influence the adequate recognition of emotions and thus the differences between the populations being compared. Although negative emotions (e.g., anger and fear) remain simpler to detect with different stimulus types, this is particularly important for positive emotions, whose adequate detection

may also depend on task-related rather than disorder-related features (Hayes et al., 2020).

Regarding recognition of sad emotional stimuli, BD patients performed faster and with more accuracy than people with SCZ. However, significant difference between the two groups was lost when two studies (Goghari and Sponheim, 2013; Rubin et al., 2022) were removed from the sensitivity analysis. Of these, the only study that showed a significant difference between the two populations (Rubin et al., 2022) included a sample of non-euthymic patients with psychotic symptoms and at least mild depression, as indicated by the scores on the depressive symptomatology rating scale. Indeed, our results suggest that an increase in scores on scales measuring depressive symptomatology predicts an increase in recognition of negative emotions in individuals with BD. This is consistent with studies in depressed patients that have described increased sensitivity to negative emotion recognition, as well as misinterpretation of ambiguous or neutral stimuli as sad (Monferrer et al., 2023), and is related to the presence of the negative cognitive biases described in these individuals (Münkler et al., 2015). Unfortunately, studies do not always provide detailed information about the mood of the patients included in their sample, making it difficult to confirm at the meta-analysis level whether this hypothesis holds when comparing BD and SCZ. Similarly, the difference between the two groups decreases as the number of BD patients treated with antipsychotics increases, suggesting that populations with more severe clinical conditions (and therefore more frequent use of antipsychotics) may have FER difficulties more similar to those of SCZ patients.

Compared with MDD patients, BD subjects showed lower accuracy in identifying facial emotional stimuli. This comparison shows zero heterogeneity, suggesting that all the individual studies point in the same direction, although none individually reaches statistical significance. Increasing statistical power is one of the goals of meta-analyses, as separate studies are often too small to detect significant differences (Higgins et al., 2019). This seems to be supported by the fact that when the largest study (Vederman et al., 2012) is removed from the latter analysis, the overall effect becomes not significant. Contrary to what was discussed above in terms of differences in neurocognition between BD and SCZ, literature directly comparing BD and MDD patients is relatively scarce and provides conflicting results (MacQueen and Memedovich, 2017). Patients with BD showed reduced (Cotrena et al., 2016; Lee et al., 2018), or similar (Hill et al., 2009) cognitive functioning compared to their controls with MDD. When considering other domains of AC, such as emotion regulation, differences between BD and MDD have been found in using specific emotion regulation strategies, including risk-taking behavior that was more prominent in BD (De Prisco et al., 2023). It is expected that the higher impulsivity during negative emotions may decrease accuracy on FER tasks, partially explaining our findings. However, the only included study that reported data on the reaction time (Derntl et al., 2012) found no significant differences between BD and MDD. Another aspect that may be considered is that antidepressants have been studied in their interaction with the amygdala, indicating that part of their action may be to modulate the balance between the processing of positive and negative emotions (Harmer and Browning, 2022). As much as this may be true in general when comparing BD and MDD and may partly help explain the difference in FER, in the few studies included in the present meta-analysis that provided us with this information, the percentage of patients taking antidepressants was about the same in the two groups.

When considering specific types of FER, people with BD showed lower accuracy than people with MDD in identifying sad emotional stimuli. Evidence of a negative bias in the recognition of facial emotional stimuli has been described extensively in MDD, suggesting the presence of subtle abnormalities (e.g., attentional biases) that may also affect social interactions (Bourke et al., 2010). These findings are also supported by neuroimaging studies in which individuals with MDD showed greater amygdala activation during recognition of sad emotional stimuli compared to their controls (Stuhrmann et al., 2013; Suslow et al., 2010). However, the presence of differences between BD and MDD could help us to better delineate the specific characteristics of the two disorders and provide an important tool for their differential diagnosis. Another aspect to consider is the mood state and, although not all studies report precise data on the mood of individual participants, it is interesting to note that the only study that showed such a significant difference, even before it was analyzed with all other studies, compared (hypo)manic BD patients with depressed MDD patients (Golkhatmi et al., 2015). As already discussed before, people experiencing depressive symptomatology may have an increased sensitivity to negative emotion recognition, and this aspect may be even more evident when comparing people experiencing two contrasting mood phases. To further support our finding, we observed that scores on scales measuring depressive symptomatology were significant predictors of accuracy in identifying positive emotions: specifically, as the depressive symptomatology of individuals with BD decreased, their ability to recognize positive emotions increased.

Children and adolescents diagnosed with BD did not significantly differ from individuals with ADHD in any of the FER stimuli considered. BD is often found in comorbidity with ADHD, even in childhood (Masi et al., 2006), so the heterogeneity in the distribution of this comorbidity could be useful in understanding the differences observed at the level of individual studies. However, given the paucity of studies in this regard, no conclusions can be drawn, and further research is needed in the child and adult populations (Torres et al., 2018), also comparing BD patients with and without ADHD comorbidity.

One aspect that emerges from this work is the great diversity of tools and tasks used to measure FER in different research protocols, a feature that may contribute to the heterogeneity observed in many comparisons. Although many studies used the same atlas from which the stimuli to be presented were drawn (Ekman, 1976), even in these cases, there were notable differences in the types of emotions presented, the number and duration of stimuli shown (ranging from 0.1 s to 15 s, when reported), the number of different actors portraying an emotional face, or the possibility of practice before the actual task. The International Society of Bipolar Disorder targeting cognition task force proposed the use of FER tests with static presentations of morphed faces at different intensities to assess emotional processing (Miskowiak et al., 2019), but only five studies among the ones included in our research used paradigms in which faces morphed from neutral or mild-intensity to full-intensity emotional expressions. All this diversity may not allow us to find real differences between the observed populations because the variety of instruments used could confound much, and future studies should try to use tasks and paradigms that are as standardized as possible to assess FER. However, we attempted to reduce this heterogeneity by including only similar tasks in our analyses and by using metaregressions to control for some specific task characteristics.

To the best of our knowledge, this is the first systematic review and meta-analysis that focuses on FER in individuals diagnosed with BD compared to other clinical populations since a previous review on the same topic was limited to the SCZ and did not examine specific types of emotional stimuli in depth (Bora and Pantelis, 2016). BD seems to be on a continuum between SCZ and MDD, as observed in other studies from a genetic perspective (Lee et al., 2019). Our findings may be useful to better understand the differences between these clinical diagnoses, which often fall within the same spectrum. Indeed, in addition to a nosographic perspective, identifying specific differences in FER may help us to highlight distinct alterations in neural connectivity patterns and allow us to better select individuals who could maximize the benefits of therapeutic strategies aimed explicitly at improving hot and cold cognition (Hook et al., 2023) in the context of precision psychiatry (Fusar-Poli et al., 2022c; Zanardi et al., 2021).

The present work has some limitations. First, there were insufficient studies to perform a meta-analysis comparing BD with clinical populations other than SCZ, MDD, and ADHD. FER has also been studied in other clinical populations diagnosed with, for example, eating disorders (Kessler et al., 2006), or borderline personality disorder (Wrege et al.,

2021), and future studies should directly address this comparison to fill the current gap in the literature. Second, the quality of the included studies was low, which may limit the conclusions suggested by our analyses. Many studies did not adequately describe their sample or clarify the statistical procedures used to calculate their sample size. In addition, they sometimes failed to match cases and controls on important confounding variables. However, the NOS score did not appear to be a potential predictor of outcome when explored through meta-regression analyses, failing to reach statistical significance in all but two comparisons that included only a few studies, limiting the strength of this finding. Third, few studies reported detailed information about the mood state of the included participants, with the majority involving people in different mood states, limiting our ability to control for the influence of mood state on FER. However, we explored this by running meta-regressions on symptom severity scales and the percentage of people experiencing specific affective symptoms. Additionally, as suggested by previous reviews comparing BD with healthy controls (Miskowiak et al., 2019), both remitted and symptomatic patients showed difficulties in FER, indicating that this impairment may be trait-related in BD. Fourth, due to its heterogeneity, we could not control for medication which was an important confounder in all the included studies (Ilzarbe and Vieta, 2023). Fourth, we could not fully control our analysis for some other confounding factors. For example, the duration of illness or the proportion of people receiving specific treatments were only reported by a proportion of the included studies so the relative metaregressions, although not significant in most cases, were limited by the few data available. In addition, few studies have controlled their results for face recognition ability in general, and our results may be partially biased by existing differences between groups in this regard. Finally, except for the comparison exploring the differences in FER accuracy between BD and SCZ, sample sizes were generally small, and few studies contributed to many comparisons, suggesting the need for more research on this topic.

5. Conclusion

People with BD are more accurate than people diagnosed with SCZ in identifying each type of emotion during a FER task, with specific differences in the perception of anger, fear, and sadness. However, people with BD were worse at identifying emotions than people with MDD, but these differences were specific to sad emotional stimuli. FER can be used to discriminate different psychiatric populations better and may be an important and potential target for uncovering novel neurobiological underpinnings that could lead to innovative targets for treatment.

CRediT authorship contribution statement

Michele De Prisco: Visualization, Data curation, Conceptualization, Methodology, Formal analysis, Software, Writing – original draft. **Vincenzo Oliva:** Visualization, Data curation, Conceptualization, Methodology, Formal analysis, Software, Writing – original draft. **Giovanna Fico:** Conceptualization, Data curation, Writing – review & editing. **Laura Montejo:** Conceptualization, Data curation, Writing – review & editing. **Chiara Possidente:** Data curation, Writing – review & editing. **Lorenzo Bracco:** Data curation, Writing – review & editing. **Lydia Fortea:** Writing – review & editing. **Gerard Anmella:** Writing – review & editing. **Diego Hidalgo-Mazzei:** Writing – review & editing. **Michele Fornaro:** Writing – review & editing. **Andrea de Bartolomeis:** Writing – review & editing. **Alessandro Serretti:** Writing – review & editing. **Andrea Murru:** Writing – review & editing. **Eduard Vieta:** Visualization, Conceptualization, Supervision, Writing – review & editing. **Joaquim Radua:** Visualization, Data curation, Conceptualization, Methodology, Supervision, Writing – review & editing.

Declaration of Competing Interest

GF has received CME-related honoraria, or consulting fees from Angelini, Janssen-Cilag and Lundbeck; GF's work is supported by a fellowship from "La Caixa" Foundation (ID 100010434 fellowship code LCF/BQ/DR21/11880019).

GA has received CME-related honoraria, or consulting fees from Janssen-Cilag, Lundbeck, Lundbeck/Otsuka, Rovi, Casen Recordati, and Angelini, with no financial or other relationship relevant to the subject of this article.

DHM has received CME-related honoraria and served as consultant for Abbott, Angelini, Ethypharm Digital Therapy and Janssen-Cilag;

MF received honoraria from the American Society of Clinical Psychopharmacology (ASCP) for his speaker activities, and from Angelini, Lundbeck, Bristol Meyer Squibb, and Boehringer-Ingelheim.

AdB has received research support from Janssen, Lundbeck, and Otsuka and lecture fees for educational meeting from Chiesi, Lundbeck, Roche, Sunovion, Vitria, Recordati, Angelini and Takeda; he has served on advisory boards for Eli Lilly, Jansen, Lundbeck, Otsuka, Roche, and Takeda, Chiesi, Recordati, Angelini, Vitria;

AS is or has been a consultant/speaker for Abbott, Abbvie, Angelini, AstraZeneca, Clinical Data, Boehringer, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Innovapharma, Italfarmaco, Janssen, Lundbeck, Naurex, Pfizer, Polifarma, Sanofi, Servier, and Taliaz;

AM has received grants and served as consultant, advisor, or CME speaker for the following entities: Angelini, Idorsia, Lundbeck, Pfizer, Takeda, outside of the submitted work;

EV has received grants and served as consultant, advisor, or CME speaker for the following entities: AB-Biotics, AbbVie, Angelini, Biogen, Biohaven, Boehringer-Ingelheim, Celon Pharma, Compass, Dainippon Sumitomo Pharma, Ethypharm, Ferrer, Gedeon Richter, GH Research, Glaxo-Smith Kline, Idorsia, Janssen, Lundbeck, Medincell, Novartis, Orion Corporation, Organon, Otsuka, Rovi, Sage, Sanofi-Aventis, Sunovion, Takeda, and Viatris, outside the submitted work;

All the other authors have no conflict to declare.

Data availability

Data will be made available on request.

Acknowledgments

GF received the support of a fellowship from "La Caixa" Foundation (ID 100010434 - fellowship code LCF/BQ/DR21/11880019). **GA** is supported by a Rio Hortega 2021 grant (CM21/00017) from the Spanish Ministry of Health financed by the Instituto de Salud Carlos III (ISCIII) and co-financed by the Fondo Social Europeo Plus (FSE+). **DHM**'s research is supported by a Juan Rodés JR18/00021 granted by the Instituto de Salud Carlos III (ISCIII). **AM** thanks the support of the Spanish Ministry of Science and Innovation (PI19/00672) integrated into the Plan Nacional de I + D + I and co-financed by the ISCIII-Subdirección General de Evaluación and the Fondo Europeo de Desarrollo Regional (FEDER). **EV** thanks the support of the Spanish Ministry of Science and Innovation (PI18/00805, PI21/00787) integrated into the Plan Nacional de I + D + I and co-financed by the ISCIII-Subdirección General de Evaluación and the Fondo Europeo de Desarrollo Regional (FEDER); the Instituto de Salud Carlos III; the CIBER of Mental Health (CIBERSAM); the Secretaria d'Universitats i Recerca del Departament d'Economia i Coneixement (2017 SGR 1365), the CERCA Programme, and the Departament de Salut de la Generalitat de Catalunya for the PERIS grant SLT006/17/00357. Thanks the support of the European Union Horizon 2020 research and innovation program (EU.3.1.1. Understanding health, wellbeing and disease: Grant No 754907 and EU.3.1.3. Treating and managing disease: Grant No 945151). **JR** thanks the support of the Spanish Ministry of Science and Innovation (PI19/00394, CPII19/00009) integrated into the Plan Nacional de I + D + I

and co-financed by the ISCIII-Subdirección General de Evaluación and the Fondo Europeo de Desarrollo Regional (FEDER) and the Instituto de Salud Carlos III.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pnpbp.2023.110847.

References

Adámek, P., Langová, V., Horáček, J., 2022. Early-stage visual perception impairment in schizophrenia, bottom-up and back again. Schizophrenia. 8, 27.

Addington, J., Addington, D., 1998. Facial affect recognition and information processing in schizophrenia and bipolar disorder. Schizophr. Res. 32, 171–181.

Agnew-Blais, J., Danese, A., 2016. Childhood maltreatment and unfavourable clinical outcomes in bipolar disorder: a systematic review and meta-analysis. Lancet Psychiatry 3, 342–349.

Almeida, J.R., Versace, A., Mechelli, A., Hassel, S., Quevedo, K., Kupfer, D.J., et al., 2009. Abnormal amygdala-prefrontal effective connectivity to happy faces differentiates bipolar from major depression. Biol. Psychiatry 66, 451–459.

Almeida, J.R., Versace, A., Hassel, S., Kupfer, D.J., Phillips, M.L., 2010. Elevated amygdala activity to sad facial expressions: a state marker of bipolar but not unipolar depression. Biol. Psychiatry 67, 414–421.

APA, 1994. Diagnostic and Statistical Manual of Mental Disorders, 4th ed. American Psychiatric Association (APA).

APA, 2000. Diagnostic and Statistical Manual of Mental Disorders, 4th ed., text rev. American Psychiatric Association (APA).

APA, 2013. Diagnostic and Statistical Manual of Mental Disorders, 5th ed. American Psychiatric Association (APA).

Bellack, A.S., Blanchard, J.J., Mueser, K.T., 1996. Cue availability and affect perception in schizophrenia. Schizophr. Bull. 22, 535–544.

Bjertrup, A.J., Jensen, M.B., Schjodt, M.S., Parsons, C.E., Kjaerbye-Thygesen, A., Mikkelsen, R.L., et al., 2021. Cognitive processing of infant stimuli in pregnant women with and without affective disorders and the association to postpartum depression. Eur. Neuropsychopharmacol. 42, 97–109.

Bora, E., Pantelis, C., 2016. Social cognition in schizophrenia in comparison to bipolar disorder: a meta-analysis. Schizophr. Res. 175, 72–78.

Bortolato, B., Miskowiak, K.W., Köhler, C.A., Vieta, E., Carvalho, A.F., 2015. Cognitive dysfunction in bipolar disorder and schizophrenia: a systematic review of meta-analyses. Neuropsychiatr. Dis. Treat. 3111-25.

Bourke, C., Douglas, K., Porter, R., 2010. Processing of facial emotion expression in major depression: a review. Australian & New Zealand J. Psychiatry. 44, 681–696.

Branco, L.D., Cotrena, C., Ponsoni, A., Salvador-Silva, R., Vasconcellos, S.J.L., Fonseca, R.P., 2018. Identification and perceived intensity of facial expressions of emotion in bipolar disorder and major depression. Arch. Clin. Neuropsychol. 33, 491–501.

Cochran, W.G., 1950. The comparison of percentages in matched samples. Biometrika. 37, 256–266.

Cotrena, C., Branco, L.D., Shansis, F.M., Fonseca, R.P., 2016. Executive function impairments in depression and bipolar disorder: association with functional impairment and quality of life. J. Affect. Disord. 190, 744–753.

Cullen, B., Ward, J., Graham, N.A., Deary, I.J., Pell, J.P., Smith, D.J., et al., 2016. Prevalence and correlates of cognitive impairment in euthymic adults with bipolar disorder: a systematic review. J. Affect. Disord. 205, 165–181.

Dalili, M.N., Penton-Voak, I.S., Harmer, C., Munafò, M.R., 2015. Meta-analysis of emotion recognition deficits in major depressive disorder. Psychol. Med. 45, 1135–1144.

Darke, H., Sundram, S., Cropper, S.J., Carter, O., 2021. Dynamic face processing impairments are associated with cognitive and positive psychotic symptoms across psychiatric disorders. NPJ Schizophr. 7, 36.

Daros, A.R., Ruocco, A.C., Reilly, J.L., Harris, M.S., Sweeney, J.A., 2014. Facial emotion recognition in first-episode schizophrenia and bipolar disorder with psychosis. Schizophr. Res. 153, 32–37.

De la Torre-Luque, A., Viera-Campos, A., Bilderbeck, A.C., Carreras, M.T., Vivancos, J., Diaz-Caneja, C.M., et al., 2022. Relationships between social withdrawal and facial emotion recognition in neuropsychiatric disorders. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 113, 110463.

De Prisco, M., Oliva, V., Fico, G., Fornaro, M., de Bartolomeis, A., Serretti, A., et al., 2022. Defining clinical characteristics of emotion dysregulation in bipolar disorder: a systematic review and meta-analysis. Neurosci. Biobehav. Rev. 104914.

De Prisco, M., Oliva, V., Fico, G., Radua, J., Grande, I., Roberto, N., et al., 2023. Emotion dysregulation in bipolar disorder compared to other mental illnesses: a systematic review and meta-analysis. Psychol. Med. https://doi.org/10.1017/S003329172300243X. Ahead of print.

de Siqueira, Rotenberg L., Kjærstad, H.L., Varo, C., Vinberg, M., Kessing, L.V., Lafer, B., et al., 2023. The longitudinal trajectory of emotional cognition in subgroups of recently diagnosed patients with bipolar disorder. Eur. Neuropsychopharmacol. 71, 9–24.

Derntl, B., Seidel, E.-M., Schneider, F., Habel, U., 2012. How specific are emotional deficits? A comparison of empathic abilities in schizophrenia, bipolar and depressed patients. Schizophr. Res. 142, 58–64.

Egger, M., Smith, G.D., Schneider, M., Minder, C., 1997. Bias in meta-analysis detected by a simple, graphical test. Bmj. 315, 629–634.

Ekman, P., 1976. Pictures of Facial Affect. Consulting Psychologists Press.

Ekman, P., Friesen, W.V., 1971. Constants across cultures in the face and emotion. J. Pers. Soc. Psychol. 17, 124.

Elfenbein, H.A., Ambady, N., 2002. On the universality and cultural specificity of emotion recognition: a meta-analysis. Psychol. Bull. 128, 203.

Elliott, R., Zahn, R., Deakin, J., Anderson, I.M., 2011. Affective cognition and its disruption in mood disorders. Neuropsychopharmacology. 36, 153–182.

Fares-Otero, N.E., De Prisco, M., Oliva, V., Radua, J., Halligan, S.L., Vieta, E., et al., 2023. Association between childhood maltreatment and social functioning in individuals with affective disorders: a systematic review and meta-analysis. Acta Psychiatr 148, 142–164.

Fico, G., Oliva, V., De Prisco, M., Giménez-Palomo, A., Sagué-Vilavella, M., Gomes-da-Costa, S., et al., 2022. The U-shaped relationship between parental age and the risk of bipolar disorder in the offspring: a systematic review and meta-analysis. Eur. Neuropsychopharmacol. 60, 55–75.

Field, T.M., Woodson, R., Greenberg, R., Cohen, D., 1982. Discrimination and imitation of facial expression by neonates. Science. 218, 179–181.

Fornaro, M., Dragioti, E., De Prisco, M., Billeci, M., Mondin, A.M., Calati, R., et al., 2022. Homelessness and health-related outcomes: an umbrella review of observational studies and randomized controlled trials. BMC Med. 20, 1–19.

Fusar-Poli, L., Pries, L.-K., van Os, J., Erzin, G., Delespaul, P., Kenis, G., et al., 2022a. Examining facial emotion recognition as an intermediate phenotype for psychosis: findings from the EUGEI study. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 113, 110440.

Fusar-Poli, L., Pries, L.-K., Van Os, J., Radhakrishnan, R., Pençe, A.Y., Erzin, G., et al., 2022b. The association between cannabis use and facial emotion recognition in schizophrenia, siblings, and healthy controls: results from the EUGEI study. Eur. Neuropsychopharmacol. 63, 47–59.

Fusar-Poli, P., Manchia, M., Koutsouleris, N., Leslie, D., Woopen, C., Calkins, M.E., et al., 2022c. Ethical considerations for precision psychiatry: a roadmap for research and clinical practice. Eur. Neuropsychopharmacol. 63, 17–34.

Goghari, V.M., Sponheim, S.R., 2013. More pronounced deficits in facial emotion recognition for schizophrenia than bipolar disorder. Compr. Psychiatry 54, 388–397.

Golkhatmi, S.H.S., Homayoni, S., Bakhshani, N.M., Sadjadi, S., Asl, M.S., 2015. A comparative study of the ability of facial emotional expression recognition and its relationship with communication skills in Iranian patients with mood disorders. Galen Med. J. 4, 90–99.

Green, M.F., Horan, W.P., Lee, J., 2019. Nonsocial and social cognition in schizophrenia: current evidence and future directions. World Psychiatry 18, 146–161.

Guo, H., Ye, H., Li, Z., Li, X., Huang, W., Yang, Y., et al., 2023. Amygdala signal abnormality and cognitive impairment in drug-naïve schizophrenia. BMC Psychiatry. 23, 1–7.

Guyer, A.E., McClure, E.B., Adler, A.D., Brotman, M.A., Rich, B.A., Kimes, A.S., et al., 2007. Specificity of facial expression labeling deficits in childhood psychopathology. J. Child Psychol. Psychiatry 48, 863–871.

Harmer, C.J., Browning, M., 2022. Emotional cognition in depression: is it relevant for clinical practice? Eur. Neuropsychopharmacol. 56, 1–3.

Harville, D.A., 1977. Maximum likelihood approaches to variance component estimation and to related problems. J. Am. Stat. Assoc. 72, 320–338.

Hayes, G.S., McLennan, S.N., Henry, J.D., Phillips, L.H., Terrett, G., Rendell, P.G., et al., 2020. Task characteristics influence facial emotion recognition age-effects: a meta-analytic review. Psychol. Aging 35, 295.

Hébert, M., Mérette, C., Gagné, A.-M., Paccalet, T., Moreau, I., Lavoie, J., et al., 2020. The electroretinogram may differentiate schizophrenia from bipolar disorder. Biol. Psychiatry 87, 263–270.

Herba, C., Phillips, M., 2004. Annotation: development of facial expression recognition from childhood to adolescence: Behavioural and neurological perspectives. J. Child Psychol. Psychiatry 45, 1185–1198.

Higgins, J.P., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M.J., et al., 2019. Cochrane Handbook for Systematic Reviews of Interventions. John Wiley & Sons.

Hill, S.K., Reilly, J.L., Harris, M.S., Rosen, C., Marvin, R.W., DeLeon, O., et al., 2009. A comparison of neuropsychological dysfunction in first-episode psychosis patients with unipolar depression, bipolar disorder, and schizophrenia. Schizophr. Res. 113, 167–175.

Ho, N.F., Chong, P.L.H., Lee, D.R., Chew, Q.H., Chen, G., Sim, K., 2019. The amygdala in schizophrenia and bipolar disorder: a synthesis of structural MRI, diffusion tensor imaging, and resting-state functional connectivity findings. Harvard Rev. P'sychiatry. 27, 150–164.

Hook, R.W., Isobe, M., Savulich, G., Grant, J.E., Ioannidis, K., Christmas, D., et al., 2023. Role of adenosine A2A receptors in hot and cold cognition: effects of single-dose istradefylline in healthy volunteers. Eur. Neuropsychopharmacol. 71, 55–64.

Hwang, H.C., Kim, S.M., Han, D.H., 2021. Different facial recognition patterns in schizophrenia and bipolar disorder assessed using a computerized emotional perception test and fMRI. J. Affect. Disord. 279, 83–88.

Ilzarbe, L., Vieta, E., 2023. The elephant in the room: medication as confounder. Eur. Neuropsychopharmacol. J. Eur. College Neuropsychopharmacol. 71, 6–8.

Jimenez, E., Sole, B., Arias, B., Mitjans, M., Varo, C., Reinares, M., et al., 2018. Characterizing decision-making and reward processing in bipolar disorder: a cluster analysis. Eur. Neuropsychopharmacol. 28, 863–874.

Kessler, H., Schwarze, M., Filipic, S., Traue, H.C., von Wietersheim, J., 2006. Alexithymia and facial emotion recognition in patients with eating disorders. Int. J. Eat. Disord. 39, 245–251.

Kohler, C.G., Walker, J.B., Martin, E.A., Healey, K.M., Moberg, P.J., 2010. Facial emotion perception in schizophrenia: a meta-analytic review. Schizophr. Bull. 36, 1009–1019.
Lahera, G., Herrera, S., Reinares, M., Benito, A., Rullas, M., Gonzalez-Cases, J., et al., 2015. Hostile attributions in bipolar disorder and schizophrenia contribute to poor social functioning. Acta Psychiatr. Scand. 131, 472–482.
Lee, J., Altshuler, L., Glahn, D.C., Miklowitz, D.J., Ochsner, K., Green, M.F., 2013. Social and nonsocial cognition in bipolar disorder and schizophrenia: relative levels of impairment. Am. J. Psychiatr. 170, 334–341.
Lee, C.-Y., Wang, L.-J., Lee, Y., Hung, C.-F., Huang, Y.-C., Lee, M.-I., et al., 2018. Differentiating bipolar disorders from unipolar depression by applying the brief assessment of cognition in affective disorders. Psychol. Med. 48, 929–938.
Lee, P.H., Anttila, V., Won, H., Feng, Y.-C.A., Rosenthal, J., Zhu, Z., et al., 2019. Genomic relationships, novel loci, and pleiotropic mechanisms across eight psychiatric disorders. Cell. 179 (1469–82), e11.
Lelli-Chiesa, G., Kempton, M.J., Jogia, J., Tatarelli, R., Girardi, P., Powell, J., et al., 2011. The impact of the Val158Met catechol-O-methyltransferase genotype on neural correlates of sad facial affect processing in patients with bipolar disorder and their relatives. Psychol. Med. 41, 779–788.
Lima, C.N.C., Suchting, R., Scaini, G., Cuellar, V.A., Favero-Campbell, A.D., Walss-Bass, C., et al., 2022. Epigenetic GrimAge acceleration and cognitive impairment in bipolar disorder. Eur. Neuropsychopharmacol. 62, 10–21.
Lopes, P.N., Salovey, P., Côté, S., Beers, M., Petty, R.E., 2005. Emotion regulation abilities and the quality of social interaction. Emotion. 5, 113.
Maat, A., van Montfort, S.J., de Nijs, J., Derks, E.M., Kahn, R.S., Linszen, D.H., et al., 2015. Emotion processing in schizophrenia is state and trait dependent. Schizophr. Res. 161, 392–398.
MacQueen, G.M., Memedovich, K.A., 2017. Cognitive dysfunction in major depression and bipolar disorder: a ssessment and treatment options. Psychiatry Clin. Neurosci. 71, 18–27.
Masi, G., Perugi, G., Toni, C., Millepiedi, S., Mucci, M., Bertini, N., et al., 2006. Attention-deficit hyperactivity disorder–bipolar comorbidity in children and adolescents. Bipolar Disord. 8, 373–381.
Matheson, S., Shepherd, A.M., Pinchbeck, R., Laurens, K., Carr, V.J., 2013. Childhood adversity in schizophrenia: a systematic meta-analysis. Psychol. Med. 43, 225–238.
McClure, E.B., Pope, K., Hoberman, A.J., Pine, D.S., Leibenluft, E., 2003. Facial expression recognition in adolescents with mood and anxiety disorders. Am. J. Psychiatr. 160, 1172–1174.
Merikangas, K.R., Jin, R., He, J.-P., Kessler, R.C., Lee, S., Sampson, N.A., et al., 2011. Prevalence and correlates of bipolar spectrum disorder in the world mental health survey initiative. Arch. Gen. Psychiatry 68, 241–251.
Miskowiak, K.W., Seeberg, I., Kjaerstad, H.L., Burdick, K.E., Martinez-Aran, A., del Mar, Bonnin C., et al., 2019. Affective cognition in bipolar disorder: a systematic review by the ISBD targeting cognition task force. Bipolar Disord. 21, 686–719.
Mitchell, A.E., Dickens, G.L., Picchioni, M.M., 2014. Facial emotion processing in borderline personality disorder: a systematic review and meta-analysis. Neuropsychol. Rev. 24, 166–184.
Monferrer, M., García, A.S., Ricarte, J.J., Montes, M.J., Fernández-Caballero, A., Fernández-Sotos, P., 2023. Facial emotion recognition in patients with depression compared to healthy controls when using human avatars. Sci. Rep. 13, 6007.
Mourao-Miranda, J., Almeida, J.R., Hassel, S., de Oliveira, L., Versace, A., Marquand, A. F., et al., 2012. Pattern recognition analyses of brain activation elicited by happy and neutral faces in unipolar and bipolar depression. Bipolar Disord. 14, 451–460.
Münkler, P., Rothkirch, M., Dalati, Y., Schmack, K., Sterzer, P., 2015. Biased recognition of facial affect in patients with major depressive disorder reflects clinical state. PLoS One 10, e0129863.
Navarra-Ventura, G., Vicent-Gil, M., Serra-Blasco, M., Massons, C., Crosas, J.M., Cobo, J., et al., 2021. Group and sex differences in social cognition in bipolar disorder, schizophrenia/schizoaffective disorder and healthy people. Compr. Psychiatry 109, 152258.
Oliva, V., Fanelli, G., Kasper, S., Zohar, J., Souery, D., Montgomery, S., et al., 2021. Social withdrawal as a trans-diagnostic predictor of short-term remission: a meta-analysis of five clinical cohorts. Int. Clin. Psychopharmacol. 37, 38–45.
Olkin, I., Dahabreh, I.J., Trikalinos, T.A., 2012. GOSH–a graphical display of study heterogeneity. Res. Synth. Methods 3, 214–223.
Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D., The PRISMA 2020, et al., 2021. Statement: an updated guideline for reporting systematic reviews. Bmj. 372.
Pollak, S.D., Sinha, P., 2002. Effects of early experience on children's recognition of facial displays of emotion. Dev. Psychol. 38, 784.
Pollak, S.D., Messner, M., Kistler, D.J., Cohn, J.F., 2009. Development of perceptual expertise in emotion recognition. Cognition. 110, 242–247.
Priyesh, C., Suryavanshi, C.A., Sasidharan, A., Bhandary, R., Behere, R.V., Nayak, K.R., 2022. Facial emotion recognition, misattribution, and response time in schizophrenia and bipolar disorder. Neurophysiology. 53, 120–131.
Quide, Y., Wilhelmi, C., Green, M.J., 2020. Structural brain morphometry associated with theory of mind in bipolar disorder and schizophrenia. Psychiatry J. 9, 234–246.
R Core Team, 2020. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria.
Ramírez-Martín, A., Ramos-Martín, J., Mayoral-Cleries, F., Moreno-Küstner, B., Guzman-Parra, J., 2020. Impulsivity, decision-making and risk-taking behaviour in bipolar disorder: a systematic review and meta-analysis. Psychol. Med. 50, 2141–2153.
Reavis, E.A., Lee, J., Wynn, J.K., Engel, S.A., Jimenez, A.M., Green, M.F., 2017. Cortical thickness of functionally defined visual areas in schizophrenia and bipolar disorder. Cereb. Cortex 27, 2984–2993.
Rey, G., Bolton, T.A., Gaviria, J., Piguet, C., Preti, M.G., Favre, S., et al., 2021. Dynamics of amygdala connectivity in bipolar disorders: a longitudinal study across mood states. Neuropsychopharmacology. 46, 1693–1701.
Roddy, D., Kelly, J.R., Farrell, C., Doolin, K., Roman, E., Nasa, A., et al., 2021. Amygdala substructure volumes in major depressive disorder. NeuroImage: Clin. 31, 102781.
Roiser, J.P., Sahakian, B.J., 2013. Hot and cold cognition in depression. CNS Spectrums. 18, 139–149.
Romani, M., Vigliante, M., Faedda, N., Rossetti, S., Pezzuti, L., Guidetti, V., et al., 2018. Face memory and face recognition in children and adolescents with attention deficit hyperactivity disorder: a systematic review. Neurosci. Biobehav. Rev. 89, 1–12.
Rossell, S.L., Van Rheenen, T.E., Joshua, N.R., O'Regan, A., Gogos, A., 2014. Investigating facial affect processing in psychosis: a study using the comprehensive affective testing system. Schizophr. Res. 157, 55–59.
Rowland, J.E., Hamilton, M.K., Vella, N., Lino, B.J., Mitchell, P.B., Green, M.J., 2012. Adaptive associations between social cognition and emotion regulation are absent in schizophrenia and bipolar disorder. Front. Psychol. 3, 607.
Rubin, L.H., Han, J., Coughlin, J.M., Hill, S.K., Bishop, J.R., Tamminga, C.A., et al., 2022. Real-time facial emotion recognition deficits across the psychosis spectrum: a B-SNIP study. Schizophr. Res. 243, 489–499.
Ruihua, M., Meng, Z., Nan, C., Panqi, L., Hua, G., Sijia, L., et al., 2021. Differences in facial expression recognition between unipolar and bipolar depression. Front. Psychol. 12, 619368.
Ruocco, A.C., Reilly, J.L., Rubin, L.H., Daros, A.R., Gershon, E.S., Tamminga, C.A., et al., 2014. Emotion recognition deficits in schizophrenia-spectrum disorders and psychotic bipolar disorder: findings from the bipolar-schizophrenia network on intermediate phenotypes (B-SNIP) study. Schizophr. Res. 158, 105–112.
Sagliano, L., Ponari, M., Conson, M., Trojano, L., 2022. The interpersonal effects of emotions: The influence of facial expressions on social interactions. Front. Psychol. 13.
Schaefer, K.L., Baumann, J., Rich, B.A., Luckenbaugh, D.A., Zarate Jr., C.A., 2010. Perception of facial emotion in adults with bipolar or unipolar depression and controls. J. Psychiatr. Res. 44, 1229–1235.
Schutte, N.S., Malouff, J.M., Bobik, C., Coston, T.D., Greeson, C., Jedlicka, C., et al., 2001. Emotional intelligence and interpersonal relations. J. Soc. Psychol. 141, 523–536.
Seymour, K.E., Pescosolido, M.F., Reidy, B.L., Galvan, T., Kim, K.L., Young, M., et al., 2013. Emotional face identification in youths with primary bipolar disorder or primary attention-deficit/hyperactivity disorder. J. Am. Acad. Child Adolesc. Psychiatry 52 (537–46), e3.
Šimić, G., Tkalčić, M., Vukić, V., Mulc, D., Španić, E., Šagud, M., et al., 2021. Understanding emotions: origins and roles of the amygdala. Biomolecules. 11, 823.
Stang, A., 2010. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur. J. Epidemiol. 25, 603–605.
Stroup, D.F., Berlin, J.A., Morton, S.C., Olkin, I., Williamson, G.D., Rennie, D., et al., 2000. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Jama. 283, 2008–2012.
Stuhrmann, A., Dohm, K., Kugel, H., Zwanzger, P., Redlich, R., Grotegerd, D., et al., 2013. Mood-congruent amygdala responses to subliminally presented facial expressions in major depression: associations with anhedonia. J. Psychiatry Neurosci. 38, 249–258.
Suslow, T., Konrad, C., Kugel, H., Rumstadt, D., Zwitserlood, P., Schöning, S., et al., 2010. Automatic mood-congruent amygdala responses to masked facial expressions in major depression. Biol. Psychiatry 67, 155–160.
Thonse, U., Behere, R.V., Praharaj, S.K., Sharma, P., 2018. Facial emotion recognition, socio-occupational functioning and expressed emotions in schizophrenia versus bipolar disorder. Psychiatry Res. 264, 354–360.
Torres, I., Garriga, M., Sole, B., Bonnín, C.M., Corrales, M., Jiménez, E., et al., 2018. Functional impairment in adult bipolar disorder with ADHD. J. Affect. Disord. 227, 117–125.
Van Rheenen, T.E., Ganella, E.P., Bauer, I.E., Bartholomeusz, C.F., 2019. Characterization of social cognitive deficits on the schizophrenia-bipolar disorder spectrum: an overview of current evidence. Soc. Cognit. Psychosis. 1–36.
Varo, C., Jiménez, E., Solé, B., Bonnín, C., Torrent, C., Lahera, G., et al., 2019. Social cognition in bipolar disorder: the role of sociodemographic, clinical, and neurocognitive variables in emotional intelligence. Acta Psychiatr. Scand. 139, 369–380.
Varo, C., Amoretti, S., Sparacino, G., Jiménez, E., Solé, B., del Mar, Bonnin C., et al., 2022. Emotional intelligence: a comparison between patients after first episode mania and those suffering from chronic bipolar disorder type I. Psychol. Med. 1-12.
Vaskinn, A., Sundet, K., Friis, S., Simonsen, C., Birkenaes, A., Engh, J., et al., 2007. The effect of gender on emotion perception in schizophrenia and bipolar disorder. Acta Psychiatr. Scand. 116, 263–270.
Vederman, A.C., Weisenbach, S.L., Rapport, L.J., Leon, H.M., Haase, B.D., Franti, L.M., et al., 2012. Modality-specific alterations in the perception of emotional stimuli in bipolar disorder compared to healthy controls and major depressive disorder. Cortex. 48, 1027–1034.
Viechtbauer, W., Viechtbauer, M.W., 2015. Package 'metafor'. The Comprehensive R Archive Network Package 'metafor'. http://cranr-projectorg/web/packages/metafor/metafor.pdf.
Vieta, E., Berk, M., Schulze, T.G., Carvalho, A.F., Suppes, T., Calabrese, J.R., et al., 2018. Bipolar disorders. Nat. Rev. Dis. Prim. 4, 1–16.
WHO, 2004. ICD-10 : International Statistical Classification of Diseases and Related Health Problems : Tenth Revision. World Health Organization (WHO).
Wrege, J.S., Ruocco, A.C., Carcone, D., Lang, U.E., Lee, A.C., Walter, M., 2021. Facial emotion perception in borderline personality disorder: differential neural activation

to ambiguous and threatening expressions and links to impairments in self and interpersonal functioning. J. Affect. Disord. 284, 126–135.
Wynn, J.K., Jahshan, C., Altshuler, L.L., Glahn, D.C., Green, M.F., 2013. Event-related potential examination of facial affect processing in bipolar disorder and schizophrenia. Psychol. Med. 43, 109–117.
Xu, P., Peng, S., Luo, Y.-j., Gong, G., 2021. Facial expression recognition: a meta-analytic review of theoretical models and neuroimaging evidence. Neurosci. Biobehav. Rev. 127, 820–836.
Yalcin-Siedentopf, N., Hoertnagl, C.M., Biedermann, F., Baumgartner, S., Deisenhammer, E.A., Hausmann, A., et al., 2014. Facial affect recognition in symptomatically remitted patients with schizophrenia and bipolar disorder. Schizophr. Res. 152, 440–445.
Zanardi, R., Prestifilippo, D., Fabbri, C., Colombo, C., Maron, E., Serretti, A., 2021. Precision psychiatry in clinical practice. Int. J. Psychiatry Clin. Pract. 25, 19–27.