



Defining clinical characteristics of emotion dysregulation in bipolar disorder: A systematic review and meta-analysis

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ABSTRACT

Emotion dysregulation (ED) is characterized by rigid and frequent use of maladaptive emotion regulation (ER) strategies. Conceptualized as a transdiagnostic feature, ED may occur in both clinical and non-clinical populations, including people diagnosed with bipolar disorder (BD) and their first-degree relatives (FDRs), though expected to manifest with differential clinical features. To this end, we conducted a systematic review and meta-analysis of the literature comparing people with BD to healthy controls (HCs) or FDRs, from inception up to November 25, 2021, across major databases. Random-effects meta-analyses considered twenty-eight studies assessing ER/ED with a validated scale. Patients with BD differed from HCs in adopting more maladaptive ER strategies, such as rumination, risk-taking behaviors, negative focus, and less adaptive ones. Unaffected FDRs differed from people with BD, yet to a lower extent, suggesting that ED may span a continuum. ED in BD should be widely explored to better understand its course and management, with specific interventions aimed at reducing its burden on both high-risk and full-threshold populations.

1. Introduction

Bipolar Disorder (BD) is a severe chronic mental illness defined by the presence of acute manic, hypomanic, depressive, or mixed episodes spaced by inter-critical periods of absent or sub-syndromic symptomatology. Its lifetime prevalence is estimated between 0.6% and 2.4% worldwide (Merikangas et al., 2011), and converging genetic, epigenetic, and environmental factors are believed to influence its onset and progression (Vieta et al., 2018). People diagnosed with BD have frequent emotional fluctuations and spend long time being symptomatic experiencing major acute or minor affective episodes (Judd et al., 2003, 2002). Such circumstances encourage these individuals to implement a series of strategies that are part of the process of emotion regulation (ER), aimed at controlling their emotional state (Koenders et al., 2020). ER is the ability of an individual to monitor, evaluate or modify emotional reactions, especially in their intensity or temporality features, to accomplish a goal (Gross, 2015; Thompson, 1994). There are many ways in

which an individual can regulate his own emotions and, depending on the behavior adopted, these strategies are classified as adaptive (i.e., cognitive reframing, acceptance, active coping) or maladaptive (i.e., negative or positive rumination, negative focus, suppression) (Dodd et al., 2019). The presence of patterns of emotional experience or emotional expression that interfere with goal-directed activity (Thompson, 2019), due to rigid or mostly maladaptive ER strategies (D'Agostino et al., 2017), leads to emotion dysregulation (ED). ED is a multidimensional and transdiagnostic construct (Kring, 2008) that includes difficulties in controlling impulsive behaviors or modulating emotional responses to negative emotions (Gratz and Roemer, 2004), abrupt or excessively slow changes in emotions (Cole and Hall, 2008), and higher levels of affective instability, with a slower return to an emotional baseline (Ebner-Priemer et al., 2015). Traumatic early life experiences, personality traits, or neurobiological factors may impact the effective ER in patients with BD (Koenders et al., 2020), who are therefore particularly susceptible to ED. In addition, they may present

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alterations in cortical (prefrontal and orbitofrontal cortex) and subcortical (amygdala and hypothalamus) brain regions that are involved in emotional perception, integration, and its behavioral translation (Bigot et al., 2020; Green and Malhi, 2006). From a clinical perspective, ED may increase the severity of manic symptoms and residual depressive symptoms (Rucklidge, 2006). Also, BD patients may present ED in euthymia (i.e. non-acute phases), as they also tend to adopt maladaptive ER strategies (Dodd et al., 2019), and present more difficulties in regulating positive emotions (Gruber, 2011) compared with healthy controls (HCs). Due to its relationship with sleep disorders, circadian rhythmicity, and suicidality (Palagini et al., 2019), ED could worsen the clinical course of BD, affect psychosocial functioning (Van Rheenen and Rossell, 2014), and quality of life (Hoertnagl et al., 2011), hence requiring specific treatment strategies (Dadomo et al., 2016). Thus, an ED assessment in BD is fundamental considering that it is a core feature of BD, and that ER holds the potential of being a target of tailored interventions.

Unfortunately, an univocal and shared definition of ED has not yet been given (D'Agostino et al., 2017), and a comprehensive view on this issue is difficult as previously acknowledged in other clinical settings (Shaw et al., 2014). To partly address this problem, numerous tools were developed providing a focus on specific aspects of ED. For example, the Cognitive Emotion Regulation Questionnaire (CERQ) (Garnefski and Kraaij, 2007) gives a measure of both maladaptive and adaptive ER strategies like self-blame, negative rumination, or acceptance, the Response to Positive Affect (RPA) scale (Feldman et al., 2008) focuses on positive rumination and dampening, while the Difficulties in Emotion Regulation Scale (DERS) (Gratz and Roemer, 2004) tries to measure the struggle in regulating negative emotions.

Despite the relevance of the topic, no systematic review and meta-analysis focusing on multiple aspects of ED in people diagnosed with BD have been performed. The present study aims at outlining and quantifying which ER strategies or ED features, assessed with an objective validated tool, allow differentiating individuals with BD from non-clinical populations such as HCs or their unaffected first-degree relatives (FDRs).

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 CRD42021293357). No modifications were made to the review protocol during the review process.

2.1. Eligibility criteria and study outcomes

We considered eligible for inclusion those original studies providing quantitative data on ER and/or ED, measured with a validated scale, in people diagnosed with BD and compared with non-clinical groups (HCs or FDRs). Psychiatric diagnoses, or their absence for non-clinical groups, had to be performed 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 restrictions about sample size or language were applied. Both observational and interventional studies were eligible for inclusion, but only baseline data were considered. Whenever multiple studies considered overlapping study populations, the largest one with the most complete data relevant to our objectives was included. Reviews, case reports, case series, and studies conducted on animals were excluded, since they do not offer a reliable control group, or include a population not considered by our criteria.

2.2. Search strategy

The PubMed/MEDLINE, EMBASE, Scopus, and PsycINFO databases were systematically searched from inception until November 25, 2021. Search strings are available for consultation in [Supplementary Materials n.1](#). The references of each included study, textbooks, and other material were hand-searched to identify potential additional studies not captured by the original search string.

2.3. Study selection and data extraction

Two authors (MDP and VO) independently screened for eligibility the retrieved titles and abstracts, and the potentially relevant studies were further independently appraised at the full-text phase by the same two authors (MDP and VO). Whenever a consensus could not be reached, a third author (AM) was consulted. The following data were extracted (when available): author(s), publication year, geographical region and country, study design, diagnostic criteria, and (semi)structured interview adopted, setting of the study, type of outcome considered, and if it was a primary or a secondary outcome, type of control group, the number of cases and controls, mean and standard deviation (SD) of the outcome for cases and controls, mean age of cases and controls, % of females among cases and controls, duration of illness among people with BD, % of people diagnosed with BD-I among cases, % of euthymic, depressed, or (hypo)manic patients among cases, % of patients under psychotropic medication among clinical groups, psychiatric or other medical comorbidities among cases and controls, and mean score obtained by cases and controls at symptom severity scales. For studies that reported data in figures only, two independent authors (MDP and VO) used WebPlotDigitizer (<https://automeris.io/WebPlotDigitizer/>) to manually extract them from figures. Where information was not available in the article, or just the abstract was available, authors were contacted up to two times to request the necessary data.

2.4. Methodological quality appraisal

The risk of bias in the included studies was independently assessed by two authors (MDP and VO), and any disagreement was resolved by a third author (AM). 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 described elsewhere (Sharmin et al., 2017).

2.5. Statistical analyses

Analyses were performed using RStudio R version 4.1.2 (R Core Team, 2020), and the meta-analysis was conducted through the metafor R-package (Viechtbauer and Viechtbauer, 2015) using a random-effect model (restricted maximum-likelihood estimator) (Harville, 1977). Effect sizes were calculated as standardized mean differences (SMD) with its confidence interval (C.I.) and represented by Hedge's g . Sensitivity analyses were conducted by removing one study at a time from the analysis; cumulative analyses were performed to evaluate the repercussions of the studies published over the years on the effect size. Heterogeneity was assessed by using the Cochran's Q test (Cochran, 1950), τ^2 and I^2 statistics (Higgins et al., 2019), and it was graphically evaluated by adopting the graphical display of study heterogeneity (GOSH) method (Olkin et al., 2012); additionally, prediction intervals were estimated (Borenstein et al., 2017). When the Cochran's Q test presented a $p < 0.05$ and the I^2 statistic showed a value $> 50\%$, a subgroup analysis was conducted according to a-priori defined subgroups whenever available (i.e., BD-type, current mood-state, type of outcome according to the original study). Publication bias was explored by visual inspection of funnel plots and using the Egger's test (Egger et al., 1997) when at least ten studies were available.

3. Results

A total of 3166 studies were identified across different sources and, after a semi-automatic duplicate removal, 1788 studies underwent further screening. Of these, 1645 were excluded at the title/abstract level, 104 after the full-text evaluation, and 5 could not be retrieved. Altogether, 34 studies were included in the present research, and 28 of them (yielding 201 comparisons) were eligible for performing a meta-analysis. Among the latter, people diagnosed with BD were compared to HCs in 28 studies (162 comparisons), and unaffected FDRs in 5 studies (39 comparisons). The PRISMA flowchart is shown in Fig. 1. Details on the excluded studies are provided in Supplementary Materials n.1.

Among the studies included in the meta-analysis, twelve of them (Becerra et al., 2016; Carruthers et al., 2022; Das et al., 2014; Ives-Deliperi et al., 2013; Linke et al., 2020; Musket et al., 2021; Oh et al., 2019; Oymak Yenilmez et al., 2021; Palagini et al., 2019; Sağlam et al., 2020; Van Rheenen et al., 2020, 2015) adopted the DERS (Gratz and Roemer, 2004), seven studies (Fletcher et al., 2013; Green et al.,

2011; Hassani and Kia, 2016; Kanske et al., 2015; Lois et al., 2017; Rowland et al., 2013; Wolkenstein et al., 2014) used the CERQ (Garnefski and Kraaij, 2007), six studies (Edge et al., 2013; Fletcher et al., 2013; Johnson et al., 2016; Peckham et al., 2016; Shapero et al., 2015; Weinstock et al., 2018) used the RPA (Feldman et al., 2008), four studies (Aslan and Baldwin, 2021; Johnson et al., 2016; Oh et al., 2019; Zhang et al., 2018) adopted the Emotion Regulation Questionnaire (ERQ) (Gross and John, 2003), four studies (Aslan and Baldwin, 2021; Oh et al., 2019; Peckham et al., 2016; Shapero et al., 2015) used the Ruminative Response Scale (RRS) (Treynor et al., 2003), and four studies (Fletcher et al., 2013; Perich et al., 2011; Van der Gucht et al., 2009; Weinstock et al., 2018) used the Response Style Questionnaire (RSQ) (Nolen-Hoeksema, 1991). It was not possible to perform a meta-analysis for those comparisons adopting the Acceptance and Action Questionnaire, II (AAQ-II) (Bond et al., 2011), the Five Factor Personality Inventory, Children (FFPI-C) (McGhee, 2007), the Global Rumination Scale (GRS) (McIntosh and Martin, 1992), the Leahy Emotional Schema Scale (LESS) (Leahy, 2002), the Life Problems Inventory (LPI) (Rathus and Miller,

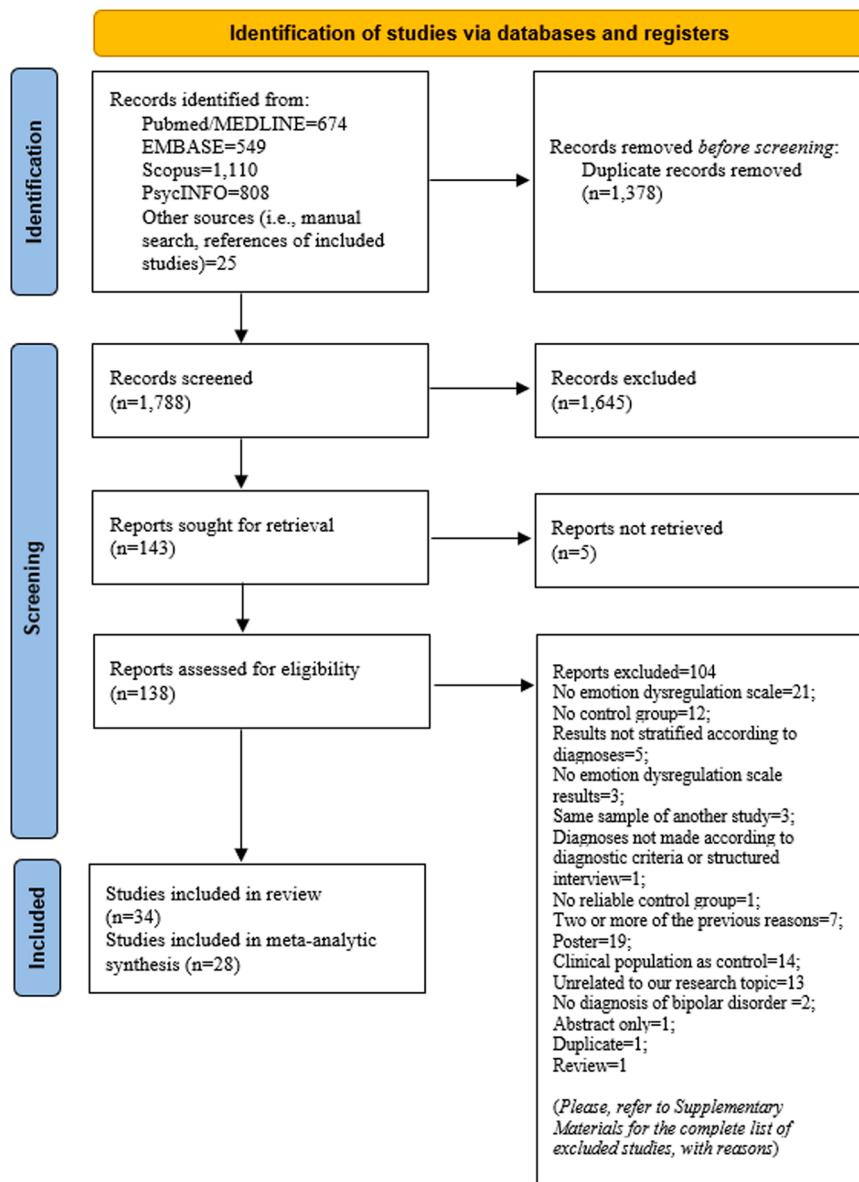


Fig. 1. PRISMA flowchart, 2020 edition.

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/>.

1995), the Negative Urgency (NU) scale (Whiteside et al., 2005), the Positive Urgency (PU) scale (Cyders et al., 2007), or the Scale of Experience of Emotions (SEE) (Behr, 2004).

Details on the studies included in the systematic review and meta-analysis are presented in Table. 1 and in Supplementary Materials n.1.

3.1. Overall measures of emotion dysregulation

A total of 9 cross-sectional studies (Becerra et al., 2016; Das et al., 2014; Linke et al., 2020; Musket et al., 2021; Oh et al., 2019; Oymak Yenilmez et al., 2021; Palagini et al., 2019; Sağlam et al., 2020; Van Rheenen et al., 2020) and 1 prospective-cohort study (Ives-Deliperi et al., 2013) including 472 patients diagnosed with BD and 415 HCs explored the overall difficulties in ER among these groups. Five studies (Becerra et al., 2016; Das et al., 2014; Oh et al., 2019; Oymak Yenilmez et al., 2021; Van Rheenen et al., 2020) included only people in euthymia, one study (Palagini et al., 2019) included only depressed patients, and four studies (Ives-Deliperi et al., 2013; Linke et al., 2020; Musket et al., 2021; Sağlam et al., 2020) included a majority of euthymic patients together with others who were depressed or manic.

BD patients presented significantly higher “total” scores (SMD=0.96; 95% C.I.=0.58, 1.35; $p = 9.9e-7$; $I^2 = 85.2\%$; $\tau^2 = 0.32$; Q test $p < 0.01$) at the DERS, but by looking at the prediction intervals the comparison became not significant. By conducting sensitivity analyses, removing any of the studies or considering only good-quality ones did not change the significance and the direction of the comparison. Studies including only people in euthymia presented a lower pooled effect size than those considering people in any mood state, but this difference was not significant at the subgroup analysis. Studies whose sample was totally (Palagini et al., 2019) or partly (Sağlam et al., 2020) depressed had a higher effect size than those considering people in euthymia; compared with the latter, the study (Musket et al., 2021) with the highest percentage of manic patients had a lower SMD instead. By inspecting the GOSH plots, subsets including the Linke 2020 or Ives-Deliperi 2013 studies seemed to present higher heterogeneity and higher or lower effect size, respectively. There was no evidence of publication bias.

A total of 3 cross-sectional studies (Linke et al., 2020; Sağlam et al., 2020; Van Rheenen et al., 2020) including 145 patients diagnosed with BD and 142 unaffected FDRs explored the overall difficulties in ER among these groups. One study (Van Rheenen et al., 2020) included only people in euthymia, and two studies (Linke et al., 2020; Sağlam et al., 2020) included a majority of euthymic patients together with others who were depressed or manic.

BD patients presented significantly higher “total” scores (SMD=0.88; 95% C.I.=0.58, 1.17; $p = 6.7e-9$; $I^2 = 31.1\%$; $\tau^2 = 0.02$; Q test $p = 0.23$) at the DERS and by looking at the prediction intervals the comparison remained significant. By conducting sensitivity analyses, removing any of the studies did not change the significance and the direction of the comparison. The study including only people in euthymia presented a lower effect size than those considering people in any mood state. By inspecting the GOSH plots, subsets including the Van Rheenen 2020 study seemed to present higher heterogeneity and lower effects size than those that did not.

Additional information about the main, sensitivity, cumulative, and subgroup analyses, and the publication bias, is presented in Supplementary Materials n.1.

An overview of the following meta-analytic results is presented in Fig. 2 and Fig. 3.

3.2. Maladaptive emotion regulation strategies

3.2.1. Negative rumination

A total of 13 cross-sectional studies including 855 patients diagnosed with BD and 804 HCs explored the extent of negative rumination among these groups. Specifically, 6 studies (Green et al., 2011; Hassani and Kia, 2016; Kanske et al., 2015; Lois et al., 2017; Rowland et al., 2013;

Wolkenstein et al., 2014) used the CERQ, 4 studies (Aslan and Baldwin, 2021; Oh et al., 2019; Peckham et al., 2016; Shapero et al., 2015) used the RRS, 2 studies (Perich et al., 2011; Van der Gucht et al., 2009) the RSQ, and 1 study (Fletcher et al., 2013) adopted both the CERQ and the RSQ. Six studies (Kanske et al., 2015; Lois et al., 2017; Oh et al., 2019; Peckham et al., 2016; Shapero et al., 2015; Wolkenstein et al., 2014) included only people in euthymia, one study (Aslan and Baldwin, 2021) included only depressed patients, and two studies (Perich et al., 2011; Van der Gucht et al., 2009) included a majority of euthymic patients together with others who were depressed or manic. The remaining studies did not provide detailed information about the mood state of people with BD.

BD patients significantly differed from HCs in all the comparisons, presenting higher scores at the “rumination” subscale of the CERQ (SMD=0.95; 95% C.I.=0.81, 1.1; $p = 2.56e-37$; $I^2 = 0\%$; $\tau^2 = 0$; Q test $p = 0.43$), at the “brooding” (SMD=0.8; 95% C.I.=0.26, 1.34; $p = 3.8e-3$; $I^2 = 83.5\%$; $\tau^2 = 0.25$; Q test $p < 0.01$), and “reflective pondering” subscales of the RRS (SMD=0.81; 95% C.I.=0.08, 1.55; $p = 0.03$; $I^2 = 89.4\%$; $\tau^2 = 0.37$; Q test $p < 0.01$), and at the “rumination” subscale of the RSQ (SMD=1.85; 95% C.I.=1.26, 2.45; $p = 1.13e-9$; $I^2 = 87.7\%$; $\tau^2 = 0.24$; Q test $p < 0.01$). By looking at the prediction intervals, all these comparisons remained significant except for the ones relative to the RRS. By conducting sensitivity analyses, removing any of the studies did not change the significance and the direction of the comparisons, except for the one relative to the “reflective pondering” subscale of the RRS in which, by removing the Oh 2019 or Shapero 2015 studies, the overall effect became not significant. Considering only good-quality studies, the comparisons remained significant, and the studies adopting the RRS presented a lower but more precise effect size. Subgroup analysis showed that among the studies exploring the differences at the “brooding” subscale, the ones including only people in euthymia presented a lower effect size compared to the one including people in any mood state, and this difference was significant. The same was observed when considering the “reflective pondering” subscale. Single studies whose sample was totally (Kanske et al., 2015; Lois et al., 2017; Wolkenstein et al., 2014) or almost totally (Perich et al., 2011) euthymic presented higher effect sizes than the others at the “rumination” subscale of the CERQ and of the RSQ, respectively. By inspecting the GOSH plots, subsets including the Fletcher 2013 study seemed to present higher heterogeneity and effect size in the comparison relative to the “rumination” subscale of the CERQ, while subsets including the Aslan 2021 study seemed to present higher heterogeneity and effect size in the comparison relative to the “brooding” subscale.

A total of 2 cross-sectional studies (Green et al., 2011; Kanske et al., 2015) including 127 patients diagnosed with BD and 141 unaffected FDRs explored the extent of negative rumination among these groups. One study (Kanske et al., 2015) included only people in euthymia, while the other did not provide detailed information about the mood state of these patients.

BD patients presented significantly higher scores at the “rumination” subscale of the CERQ (SMD=0.82; 95% C.I.=0.35, 1.29; $p = 5.9e-4$; $I^2 = 47.6\%$; $\tau^2 = 0.06$; Q test $p = 0.17$), and by looking at the prediction intervals the comparison remained significant. The single study that included only people during euthymia had a higher effect size than the other.

Additional information about the main, sensitivity, cumulative, and subgroup analyses is presented in Supplementary Materials n.1.

3.2.2. Positive rumination

A total of 3 cross-sectional (Fletcher et al., 2013; Shapero et al., 2015; Weinstock et al., 2018) and 1 prospective-cohort study (Johnson et al., 2016) including 321 patients diagnosed with BD and 406 HCs explored the extent of positive rumination among these groups. One study (Shapero et al., 2015) included only people in euthymia, and one study (Weinstock et al., 2018) included only depressed patients. The remaining studies did not provide detailed information about the mood state of

Table 1
 Characteristics of the studies included in the Systematic Review and Meta-analysis.

Author, year, country	Study design	Description of the study and population characteristics	Diagnostic criteria	Scales adopted	Emotion regulation strategy type considered	Quality of the study (NOS)
(Aslan and Baldwin, 2021), United Kingdom	Cross-sectional	Population included: 50 patients with BD, 50 patients with MDD, 50 HCs; Outcome (primary): exploring the differences between groups in terms of rumination, emotion regulation and cognitive functions; Other: patients were currently depressed. People with current psychotic symptoms, alcohol or substance abuse, or major neurological disease, were excluded	DSM-5 (SCID-5)	ERQ; RRS	Negative Rumination (RRS-1,2); Suppression (ERQ-2); Cognitive Reframing (ERQ-1)	5 / FAIR
(Barton et al., 2021), Canada	Cross-sectional	Population included: 244 young patients with BD, 146 HCs; Outcome (primary): to explore the differences among the groups in the prevalence of police contacts and its associated characteristics	DSM-IV (K-SADS-PL)	LPI	Overall emotion dysregulation (LPI, emotion dysregulation subscale)	5 / FAIR
(Batmaz et al., 2014), Turkey	Cross-sectional	Population included: 140 outpatients with BD-I, 166 outpatients with MDD, 151 HCs; Outcome (primary): to distinguish unipolar and bipolar depression in terms of metacognitions and emotional schemas; Other: patients were all depressed. People with a comorbid axis-I psychiatric condition, uncontrolled medical condition, with substance use, history of head-trauma, pregnant, or taking psychiatric treatment in the last 12 weeks, were excluded	DSM-IV	LESS	Overall maladaptive emotion regulation strategies (LESS-2,3); Adaptive coping (LESS-1)	4 / POOR
(Becerra et al., 2016), Australia	Cross-sectional	Population included: 24 patients with BD-I, 38 patients with MDD, 38 HCs; Outcome (primary): exploring the differences in emotion regulation difficulties; Other: people with BD were euthymic for at least three months. People who were pregnant, with a score on the Spielberger State/Trait Anxiety Inventory of more than 50, with a score on the MADRS of more than 5, and a score on the YMRS of more than 4, were excluded	DSM-IV (MINI)	DERS	Overall emotion dysregulation (DERS-TOT); Risk-taking (DERS-3); Adaptive coping (DERS-2,5); Acceptance (DERS-1,4,6)	5 / FAIR
(Carruthers et al., 2022), Australia	Cross-sectional	Population included: 66 outpatients with BD-I (62) or BD-II (4), 28 HCs; Outcome (primary): exploring the mediating role of emotion regulation difficulties on dispositional mindfulness and depressive or manic tendencies; Other: people who presented neurological diseases, pregnancy, visual or hearing impairment, or recent substance use, were excluded	DSM-IV (MINI)	DERS	Risk-taking (DERS-3); Adaptive coping (DERS-2,5); Acceptance (DERS-1,6)	5 / FAIR
(Das et al., 2014), Australia	Cross-sectional	Population included: 16 outpatients with BD, 14 outpatients with BPD, 13 HCs; Outcome (primary): fMRI to investigate the functional connectivity between and within brain networks subserving social cognition or emotion regulation; Other: people with BD were euthymic and mostly on medication at the time of the assessment. Patients with neurological illnesses, substance abuse, lifetime head injury or poor English proficiency, were excluded	DSM-IV	DERS	Overall emotion dysregulation (DERS-TOT); Risk-taking (DERS-3); Adaptive coping (DERS-2,5); Acceptance (DERS-1,4,6)	4 / POOR
(Edge et al., 2013), USA	Cross-sectional	Population included: 90 patients with BD-I, 72 HCs; Outcome (primary): to evaluate the diverse response to positive emotions among the groups; Other: people with substance use, psychotic symptoms, current use of antipsychotics, neurological conditions, head trauma, or developmental disabilities were excluded	DSM-IV (SCID)	RPA	Dampening (RPA-2)	5 / FAIR
(Fletcher et al., 2013), Australia	Cross-sectional	Population included: 193 patients with BD-I (86) or BD-II (107), 93 patients with MDD, 90 HCs; Outcome (primary): exploring the different coping styles in clinical and non-clinical groups	DSM-IV (MINI)	CERQ; RPA; RSQ	Negative Rumination (CERQ-3; RSQ-1); Positive Rumination (RPA-1,3); Negative Focus (CERQ-1,2,4); Risk-taking (RSQ-3); Dampening (RPA-2); Cognitive Reframing (CERQ-5,6,7,9); Adaptive Coping (RSQ-2); Acceptance (CERQ-8)	4 / POOR
(Green et al., 2011), Australia	Cross-sectional	Population included: 105 patients with BD-I, 124 FDRs, 63 HCs; Outcome (primary): exploring the differences among the	DSM-IV (DIGS)	CERQ	Negative Rumination (CERQ-3); Negative Focus (CERQ-1,2,4);	6 / GOOD

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Table 1 (continued)

Author, year, country	Study design	Description of the study and population characteristics	Diagnostic criteria	Scales adopted	Emotion regulation strategy type considered	Quality of the study (NOS)
(Gruber et al., 2008), USA	Cross-sectional	groups in adopting adaptive and maladaptive emotion regulation strategies Population included: 21 patients with BD-I, 20 HCs; Outcome (primary): to evaluate the extent of worry and rumination in people with BD and people with clinically relevant insomnia; Other: patients were all euthymic and on treatment.	DSM-IV (SCID)	GRS	Cognitive Reframing (CERQ-5,6,7,9); Acceptance (CERQ-8) Negative Rumination (GRS, total score)	6 / FAIR
(Hassani and Kia, 2016), Iran	Cross-sectional	Population included: 25 patients with BD, 25 HCs; Outcome (primary): exploring the role of cognitive emotion regulation strategies, anxiety, and impulsivity in developing and maintaining affective symptomatology	DSM-IV (CIDI)	CERQ (short version)	Negative Rumination (CERQ-3); Negative Focus (CERQ-1,2,4); Cognitive Reframing (CERQ-5,6,7,9); Acceptance (CERQ-8)	5 / FAIR
(Ives-Deliperi et al., 2013), South Africa	Prospective cohort	Population included: 23 patients with BD, 10 HCs; Outcome (primary): assessing the differences in cognitive functioning, clinical measurement of mindfulness, mood and anxiety symptoms, and brain activation in patients exposed to an eight-week mindfulness-based cognitive therapy; Other: patients were included in the study if presented mild or subthreshold affective symptoms	DSM-IV (SCID)	DERS	Overall emotion dysregulation (DERS-TOT)	4 / POOR
(Johnson et al., 2016), USA	Prospective cohort	Population included: 67 patients with BD-I, 58 HCs; Outcome (primary): exploring the extent of emotional disturbances among the groups; Other: a subgroup of patients was asked to complete a symptom severity assessment after 12 months. Lifetime substance use was diagnosed both in patients with BD (57.6%) and HCs (9.8%), as well as anxiety disorders which were diagnosed in people with BD (55.9%) and HCs (3.9%). Participants were paid for participation. People with a diagnosis of substance abuse or dependence in the past year, a general medical condition of the central nervous system, severe head trauma, or developmental or learning disabilities were excluded	DSM-IV (SCID-I)	ERQ; RPA	Positive Rumination (RPA-1,3); Suppression (ERQ-2); Dampening (RPA-2); Cognitive Reframing (ERQ-1)	4 / POOR
(Kanske et al., 2015), Germany	Cross-sectional	Population included: 22 patients with BD-I, 17 FDRs, 22 HCs; Outcome (primary): MRI scanning to investigate the activity of brain areas involved in emotion regulation; Other: patients were all euthymic and mostly on medications. Patients with current or lifetime substance use, head trauma history, or with large tattoos with metal-containing color, were excluded	DSM-IV (SCID-I)	CERQ	Negative Rumination (CERQ-3); Negative Focus (CERQ-1,2,4); Cognitive Reframing (CERQ-5,6,7,9); Acceptance (CERQ-8)	6 / GOOD
(Kelman et al., 2020), USA	Cross-sectional	Population included: 33 young outpatients with BD-I (21), BD-II (2), or BD-NOS (10), 21 HCs; Outcome (primary): to explore the differences in emotion regulation; Other: patients with BD presented several comorbidities, like ADHD (16%), ODD (16%), GAD (13%), OCD (3%), or not specified eating disorder (3%)	DSM-IV (WASH-U-KSADS)	FFPI-C	Overall emotion regulation (FFPI-C, emotional regulation subscale)	4 / POOR
(Linke et al., 2020), USA	Cross-sectional	Population included: 36 young outpatients with BD-I (15) or BD-II (21), 36 FDRs, 36 HCs; Outcome (primary): MRI to compare their white matter microstructure and to relate the difference to the difficulties in emotion regulation; Other: patients were mostly euthymic and on medication and were comorbid with other psychiatric disorder like ADHD (18) or anxiety disorders (16)	DSM-IV (K-SADS-PL)	DERS	Overall emotion dysregulation (DERS-TOT); Risk-taking (DERS-3); Adaptive coping (DERS-2,5); Acceptance (DERS-1,4,6)	5 / FAIR
(Lois et al., 2017), Germany	Cross-sectional	Population included: 21 patients with BD-I, 21 patients with MDD, 23 HCs; Outcome (primary): performing emotional tasks during fMRI scanning to explore and compare the patterns of functional connectivity during distraction and reappraisal in specific regions of interest; Other: patients were euthymic. Patients with current or lifetime substance use, head trauma history, or with large tattoos with metal-containing color, were excluded	DSM-IV (SCID)	CERQ	Negative Rumination (CERQ-3)	7 / GOOD
(Muhtadie et al., 2014), USA	Cross-sectional	Population included: 92 outpatients with BD-I, 80 HCs; Outcome (primary): to compare specific aspects of impulsivity and its relationship with psychiatric symptomatology	DSM-IV (SCID)	NU; PU	Positive Rumination (PU); Risk-taking (NU)	7 / GOOD
(Musket et al., 2021), USA	Cross-sectional	Population included: 51 outpatients with BD-I, 32 outpatients with MDD, 30 HCs;	DSM-IV (SCID-I)	DERS	Overall emotion dysregulation (DERS-	6 / GOOD

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Table 1 (continued)

Author, year, country	Study design	Description of the study and population characteristics	Diagnostic criteria	Scales adopted	Emotion regulation strategy type considered	Quality of the study (NOS)
(Oh et al., 2019), Republic of Korea	Cross-sectional	Outcome (primary): exploring the differences in difficulties in emotion regulation; Other: patients were euthymic (32) or manic (19). People with a lifetime history of neurological disease, severe head trauma, stroke, autoimmune disorder, severe medical illness, and alcohol or substance abuse in the past six months were excluded Population included: 43 outpatients with BD-I, 48 HCs; Outcome (primary): exploring the relationship between working memory capacity and emotion regulation strategies; Other: people with BD were euthymic and mostly on medication	DSM-IV (MINI)	DERS; ERQ; RRS	TOT; Risk-taking (DERS-3); Adaptive coping (DERS-2,5); Acceptance (DERS-1,4,6)	7 / GOOD
(Oymak Yenilmez et al., 2021), Turkey	Cross-sectional	Population included: 85 outpatients with BD-I (64) or BD-II (21), 81 outpatients with MDD, 86 HCs; Outcome (primary): determining the role of emotion dysregulation and childhood adversities on automatic thoughts and meta-cognition; Other: people with BD were euthymic for at least six months. People who had any central nervous system disease, intellectual disability, alcohol or any other substance use disorder, history of major traumas and head injuries, or hospitalized in the last six months, were excluded	DSM-IV (SCID-I)	DERS	Overall emotion dysregulation (DERS-TOT); Negative Rumination (RRS-1,2); Risk-taking (DERS-3); Suppression (ERQ-2); Cognitive Reframing (ERQ-1); Adaptive coping (DERS-2,5); Acceptance (DERS-1,6)	5 / FAIR
(Palagini et al., 2019), Italy	Cross-sectional	Population included: 85 inpatients with BD-II, 35 HCs; Outcome (primary): exploring the association between circadian rhythms and psychopathological symptoms, suicidality, and emotion dysregulation; Other: people with current substance use or with diagnosed with cognitive impairment, were excluded	DSM-5 (SCID-5)	DERS	Overall emotion dysregulation (DERS-TOT)	6 / GOOD
(Peckham et al., 2016), USA	Cross-sectional	Population included: 29 patients with BD-I, 28 HCs; Outcome (primary): exploring the attentional bias by the means of eye-tracking methodology, and its relationship with emotion regulation strategies; Other: patients were euthymic. People with substance use, diagnosis of a primary psychotic disorder, developmental or cognitive disabilities, colorblindness, brain injury or neurological disorders, or any history of eye injury were excluded	DSM-IV (SCID)	RPA; RRS	Negative Rumination (RRS-2); Dampening (RPA-2)	5 / FAIR
(Perich et al., 2011), Australia	Cross-sectional	Population included: 90 patients with BD, 36 patients with MDD, 66 HCs; Outcome (primary): to explore the relationship between mindfulness and psychiatric symptomatology among clinical groups; Other: patients with BD were mostly euthymic, patient with MDD were in remission. People with a diagnosis of schizophrenia or schizoaffective disorder, substance abuse disorder, organic brain syndrome, antisocial or borderline personality disorder, or a concurrent significant medical condition impeding their ability to participate, were excluded	DSM-IV (SCID)	RSQ	Negative Rumination (RSQ-1); Risk-taking (RSQ-3); Adaptive Coping (RSQ-2)	6 / FAIR
(Rowland et al., 2013), Australia	Cross-sectional	Population included: 97 patients with BD-I, 126 patients with schizophrenia, 81 HCs; Outcome (primary): exploring the differences among the groups in adopting adaptive and maladaptive emotion regulation strategies	DSM-IV (DIGS)	CERQ	Negative Rumination (CERQ-3); Negative Focus (CERQ-1,2,4); Cognitive Reframing (CERQ-5,6,7,9); Acceptance (CERQ-8)	6 / GOOD
(Sağlam et al., 2020), Turkey	Cross-sectional	Population included: 64 outpatients with BD, 64 FDRs, 66 HCs; Outcome (primary): investigating the differences among emotion regulation strategies and its effects on the affective psychopathology; Other: people with BD were both euthymic (31), depressed (21), or manic/hypomanic (12)	DSM-5 (SCID)	DERS	Overall emotion dysregulation (DERS-TOT); Risk-taking (DERS-3); Adaptive coping (DERS-2,5); Acceptance (DERS-1,4,6)	5 / POOR
(Houshmand et al., 2010), Germany	Cross-sectional	Population included: 34 outpatients with BD, 22 FDRs, 33 HCs; Outcome (primary): to investigate the performance on a	DSM-IV (SCID-I)	SEE	Overall maladaptive emotion regulation strategies (SEE-2,3,4,5);	6 / GOOD

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Table 1 (continued)

Author, year, country	Study design	Description of the study and population characteristics	Diagnostic criteria	Scales adopted	Emotion regulation strategy type considered	Quality of the study (NOS)
(Shapero et al., 2015), USA	Cross-sectional	choice-task in people under an emotional or a relaxation condition; Other: patients were all euthymic Population included: 31 young patients with BD, 122 young patients with MDD, 228 HCs; Outcome (primary): to identify and differentiate the cognitive styles among the different groups; Other: patients were all euthymic. People with lifetime history of any psychotic disorder or not fluent in English were excluded	DSM-IV (SADS-L)	RPA; RRS	Adaptive Coping (SEE-6,7); Acceptance (SEE-1) Negative Rumination (RRS-1,2); Positive Rumination (RPA-1,3); Dampening (RPA-2)	6 / GOOD
(Van der Gucht et al., 2009), United Kingdom	Cross-sectional	Population included: 107 patients with BD, 41 HCs; Outcome (primary): to examine psychological processes and reward responsivity in relation to different mood episodes and symptomatology; Other: patients were euthymic (43), depressed (30) or with manic/mixed symptomatology (34). People who had a clear organic cause for their disorder or medical comorbidity in the last 24 months that put the psychiatric diagnosis in doubt, were excluded	DSM-IV (SCID)	RSQ	Negative Rumination (RSQ-1); Risk-taking (RSQ-3); Adaptive Coping (RSQ-2)	7 / GOOD
(Van Rheenen et al., 2015), Australia	Cross-sectional	Population included: 50 outpatients with BD-I (38) or BD-II (12), 52 HCs; Outcome (primary): exploring the differences in emotion regulation difficulties; Other: people with BD were both euthymic (17), depressed (17), or manic/hypomanic (16). Patients with current substance use, visual impairment, or neurological issues, were excluded	DSM-IV (MINI)	DERS	Risk-taking (DERS-3); Adaptive coping (DERS-2,5); Acceptance (DERS-1,4,6)	6 / GOOD
(Van Rheenen et al., 2020), Australia	Cross-sectional	Population included: 45 outpatients with BD-I (43) or BD-II (2), 42 FDRs, 53 HCs; Outcome (primary): exploring the differences in emotion regulation difficulties; Other: patients were all euthymic. People with current substance use, visual impairment, pregnancy, or neurological issues, were excluded	DSM-IV (MINI)	DERS	Overall emotion dysregulation (DERS-TOT); Risk-taking (DERS-3); Adaptive coping (DERS-2,5); Acceptance (DERS-1,4,6)	5 / FAIR
(Weinstock et al., 2018), USA	Cross-sectional	Population included: 30 outpatients with BD-I, 30 outpatients with MDD, 30 HCs; Outcome (primary): exploring the differences among the groups in emotion regulation processes; Other: patients were currently depressed. People with current psychotic symptoms, alcohol or substance abuse, or major neurological disease, were excluded	DSM-IV (SCID-I)	AAQ-II; RPA; RSQ	Negative Rumination (RRS-2); Positive Rumination (RPA-1,3); Dampening (RPA-2); Acceptance (AAQ-II, total score)	5 / FAIR
(Wolkenstein et al., 2014), Germany	Cross-sectional	Population included: 42 outpatients with BD-I (26) or BD-II (16), 43 outpatients with MDD, 39 HCs; Outcome (primary): comparing the habitual use of emotion regulation strategies; Other: patients were euthymic and mostly on medications. Patients with insufficient knowledge of the german language, with lifetime psychotic symptoms, with current substance use, or with a comorbid diagnosis of personality disorders (A or B) or anorexia nervosa, were excluded	DSM-IV (SCID-I)	CERQ	Negative Rumination (CERQ-3); Negative Focus (CERQ-1,2,4); Cognitive Reframing (CERQ-5,6,7,9); Acceptance (CERQ-8)	4 / POOR
(Zhang et al., 2018), The Netherlands	Cross-sectional	Population included: 15 inpatients with BD-I (13) or BD-II (2), 14 HCs; Outcome (primary): to investigate the connectivity from the VLPFC and DLPFC to the amygdala and between the VLPFC and DLPFC during reappraisal; Other: people with BD were mostly euthymic and on medications	DSM-5 (MINI-plus)	ERQ	Suppression (ERQ-2); Cognitive Reframing (ERQ-1)	5 / FAIR

Notes:

AAQ-II - Acceptance and Action Questionnaire, II; ADHD - Attention Deficit-Hyperactivity disorder; BD - Bipolar Disorder; BPD - Borderline Personality Disorder; CERQ - Cognitive Emotion Regulation Questionnaire; CERQ-1 - Self-blame; CERQ-2 - Blaming others; CERQ-3 - Rumination; CERQ-4 - Catastrophizing; CERQ-5 - Putting into perspective; CERQ-6 - Positive Refocus; CERQ-7 - Positive Reappraisal; CERQ-8 - Acceptance; CERQ-9 - Focus on replanning; DERS - Difficulties in Emotion Regulation Scale; DERS-1 - Non acceptance; DERS-2 - Goals; DERS-3 - Impulse; DERS-4 - Awareness; DERS-5 - Strategies; DERS-6 - Clarity; DERS-TOT - Total score; DIGS - Diagnostic Interview for Genetic Studies; DLPFC - Dorsolateral prefrontal cortex; DSM - Diagnostic and Statistical Manual of Mental Disorders; ERQ - Emotion Regulation Questionnaire; ERQ-1 - Reappraisal; ERQ-2 - Suppression; FDR - First-degree relative; FFPI-C - Five Factor Personality Inventory, Children; GRS - Global Rumination Scale; HC - Healthy Controls; LESS - Leahy Emotional Schema Scale; LESS-1 - Adaptive emotional schemas; LESS-2 - Rigid emotional schemas; LESS-3 - Negative beliefs about emotions; LPI - Life Problems Inventory; MADRS - Montgomery-Asberg Depression Rating Scale; MDD - Major Depressive Disorder; MINI - The Mini-International Neuropsychiatric Interview; MRI - Magnetic resonance imaging; NOS - Newcastle-Ottawa Scale; NU - Negative Urgency scale; PU - Positive Urgency Scale; RPA - Response to Positive Affect; RPA-1 - Emotion focus; RPA-2 - Dampening; RPA-3 - Self-focus; RRS - Ruminative Response Scale; RRS-1 - Reflective Pondering; RRS-2 - Brooming; RSQ - Response Styles Questionnaire; RSQ-1 - Rumination; RSQ-2 - Adaptive; RSQ-3 - Risk-taking; SADS - Schedule for Affective Disorders and Schizophrenia; SCID - Structured Clinical Interview for DSM Disorders; SEE - Scale of Experience of Emotions; SEE-1 - Acceptance of own emotions; SEE-2 - Emotional flooding; SEE-3 - Lack of emotions; SEE-4 - Somatic expression of emotions; SEE-5 - Imaginative symbolization of emotions; SEE-6 - Regulation of emotions; SEE-7 - Self-control; VLPFC - Ventrolateral prefrontal cortex; YMRS - Young Mania Rating Scale.

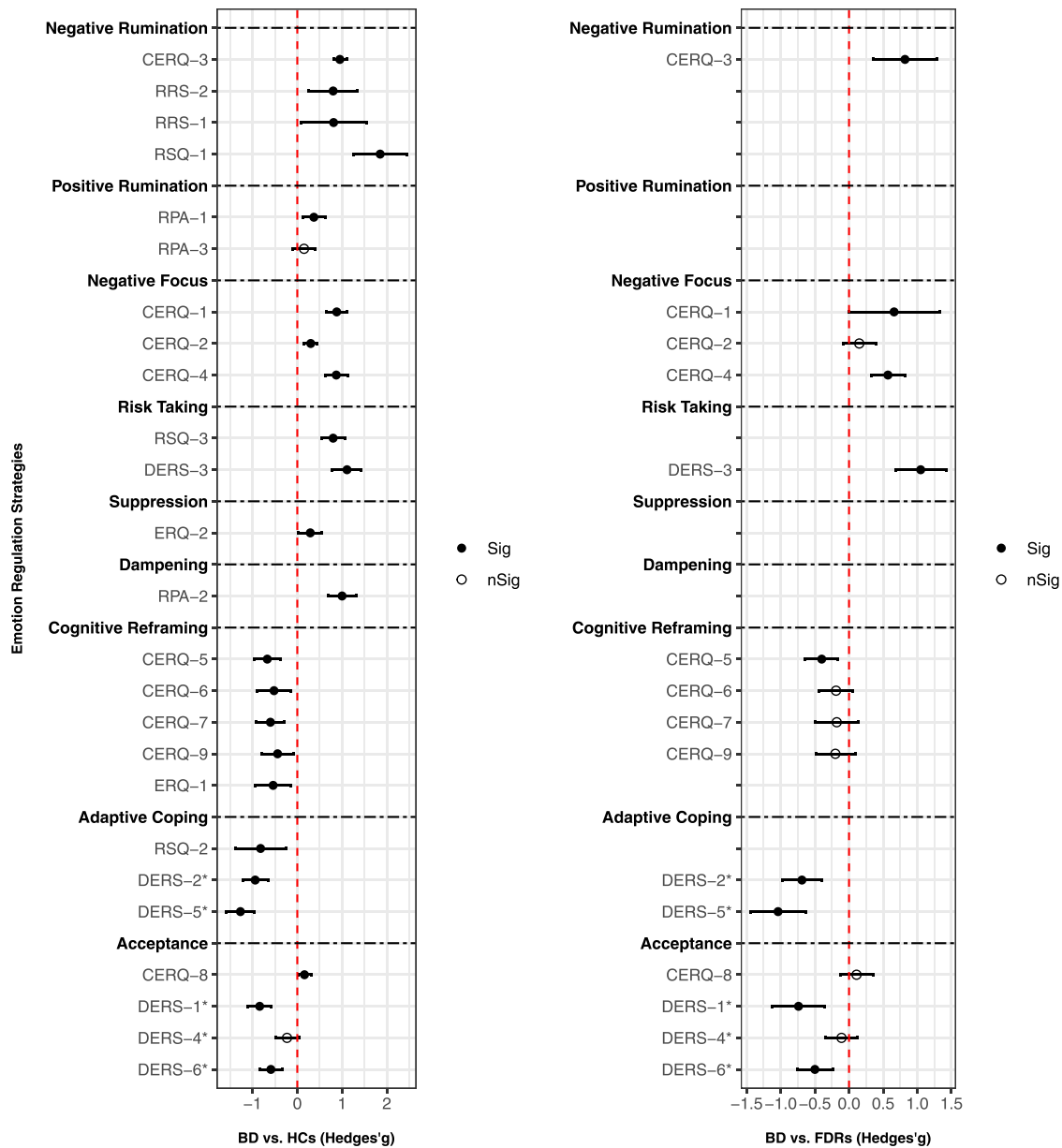


Fig. 2. Differences in adopted emotion regulation strategies between people with bipolar disorder and healthy controls (left) and first-degree relatives (right). Overall results of the comparisons included in the meta-analysis. Notes: CERQ - Cognitive Emotion Regulation Scale; CERQ-1 - Self-blame; CERQ-2 - Blaming others; CERQ-3 - Rumination; CERQ-4 - Catastrophizing; CERQ-5 - Putting into perspective; CERQ-6 - Positive Refocus; CERQ-7 - Positive Reappraisal; CERQ-8 - Acceptance; CERQ-9 - Focus on replanning; DERS - Difficulties in Emotion Regulation Scale; DERS-1 - Non acceptance; DERS-2 - Goals; DERS-3 - Impulse; DERS-4 - Awareness; DERS-5 - Strategies; DERS-6 - Clarity; ERQ - Emotion Regulation Questionnaire; ERQ-1 - Reappraisal; ERQ-2 - Suppression; FDR - First-degree relative; HC - Healthy Control; RPA - Response to Positive Affect; RPA-1 - Emotion focus; RPA-2 - Dampening; RPA-3 - Self-focus; RRS - Ruminative Response Scale; RRS-1 - Reflective Pondering; RRS-2 - Brooming; RSQ - Response Style Questionnaire; RSQ-1 - Rumination; RSQ-2 - Adaptive; RSQ-3 - Risk-taking *The effect sizes (ES) of these items have been inverted to present graphically coherent results, since the scale originally measures the individual's difficulties in adopting that emotion regulation strategy. Original ES are presented in the main text.

included samples.

BD patients presented significantly higher scores at the “*emotion-focus*” subscales of the RPA scale (SMD=0.37; 95% C.I.=0.12, 0.62; $p = 3.5e-3$; $I^2 = 48.1\%$; $\tau^2 = 0.03$; Q test $p = 0.13$). By looking at the prediction intervals, the comparison became not significant. By conducting sensitivity analysis, removing any of the studies from the comparison relative to the “*emotion-focus*” subscales did not change its significance or direction while removing the Fletcher 2013 study from the comparison relative to the “*self-focus*” subscale the overall effect became significant. Single studies including only euthymic or depressed patients presented similar effect sizes in both the comparisons. By

inspecting the GOSH plots, subsets including the Fletcher K 2013 study seemed to present higher heterogeneity and lower effect size in the comparison relative to the “*self-focus*” subscale.

Additional information about the main, sensitivity, and cumulative analyses is presented in [Supplementary Materials n.1](#).

3.2.3. Negative focus

A total of 6 cross-sectional studies (Fletcher et al., 2013; Green et al., 2011; Hassani and Kia, 2016; Kanske et al., 2015; Rowland et al., 2013; Wolkenstein et al., 2014) including 484 patients diagnosed with BD and 320 HCs explored the extent of negative focus among these groups. Two

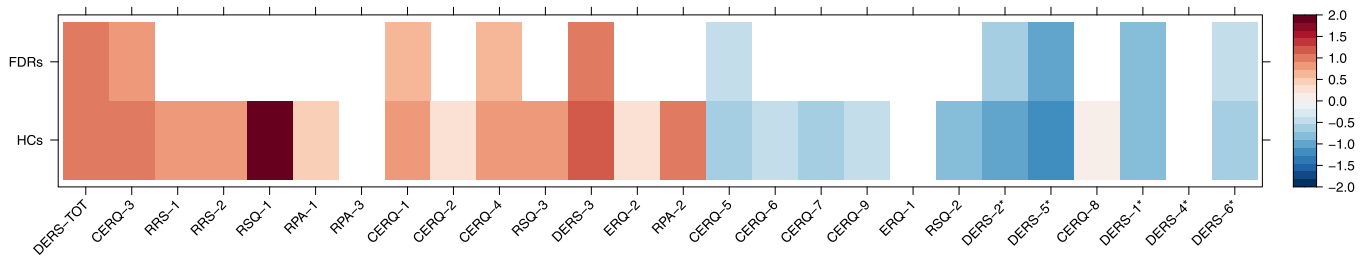


Fig. 3. Heatmap of significant effect sizes among the comparisons included in the meta-analysis. Notes: Populations: FDR - First-degree relative; HC - Healthy Control Subsamples: CERQ - Cognitive Emotion Regulation Scale; CERQ-1 - Self-blame; CERQ-2 - Blaming others; CERQ-3 - Rumination; CERQ-4 - Catastrophizing; CERQ-5 - Putting into perspective; CERQ-6 - Positive Refocus; CERQ-7 - Positive Reappraisal; CERQ-8 - Acceptance; CERQ-9 - Focus on replanning; DERS - Difficulties in Emotion Regulation Scale; DERS-1 - Non acceptance; DERS-2 - Goals; DERS-3 - Impulse; DERS-4 - Awareness; DERS-5 - Strategies; DERS-6 - Clarity; DERS-TOT - Total score; ERQ - Emotion Regulation Questionnaire; ERQ-1 - Reappraisal; ERQ-2 - Suppression; RPA - Response to Positive Affect; RPA-1 - Emotion focus; RPA-2 - Dampening; RPA-3 - Self-focus; RRS - Ruminative Response Scale; RRS-1 - Reflective Pondering; RRS-2 - Brooding; RSQ - Response Style Questionnaire; RSQ-1 - Rumination; RSQ-2 - Adaptive; RSQ-3 - Risk-taking *The effect sizes (ES) of these items have been inverted to present graphically coherent results, since the scale originally measures the individual's difficulties in adopting that emotion regulation strategy. Original ES are presented in the main text.

studies (Kanske et al., 2015; Wolkenstein et al., 2014) included only people in euthymia, while the others did not provide detailed information about the mood state of patients with BD.

BD patients presented significantly higher scores at the “self-blame” (SMD=0.88; 95% C.I.=0.68, 1.38; $p = 1.66 \times 10^{-13}$; $I^2 = 53.4\%$; $\tau^2 = 0.05$; Q test $p = 0.05$), “blaming others” (SMD=0.30; 95% C.I.=0.15, 0.44; $p = 4.88 \times 10^{-5}$; $I^2 = 0\%$; $\tau^2 = 0$; Q test $p = 0.59$), and “catastrophizing” subscales of the CERQ (SMD=0.87; 95% C.I.=0.62, 1.12; $p = 1.09 \times 10^{-11}$; $I^2 = 59.5\%$; $\tau^2 = 0.05$; Q test $p = 0.02$). By looking at the prediction intervals, all the comparisons remained significant. By conducting sensitivity analyses, removing any of the studies, or considering just good-quality ones did not change the significance and the direction of the comparisons. Subgroup analysis showed that among the meta-analyses with significant heterogeneity, the studies including only people diagnosed with BD-I presented a lower effect size and reduced heterogeneity than the ones including people diagnosed with any type of BD. Instead, studies that included only people in euthymia had a higher effect size when compared with the others, but this difference was not significant. By inspecting the GOSH plots, subsets including the Fletcher2013 study seemed to present, in all the previous comparisons, higher heterogeneity and effect size.

A total of 2 cross-sectional studies (Green et al., 2011; Kanske et al., 2015) including 127 patients diagnosed with BD and 141 unaffected FDRs explored the extent of negative focus among these groups. One study (Kanske et al., 2015) included only people in euthymia, while the other did not provide detailed information about the mood state of these patients.

BD patients presented significantly higher scores at the “self-blame” (SMD=0.66; 95% C.I.=0, 1.33; $p = 0.05$; $I^2 = 71.3\%$; $\tau^2 = 0.17$; Q test $p = 0.06$), and “catastrophizing” subscales of the CERQ (SMD=0.57; 95% C.I.=0.33, 0.82; $p = 5 \times 10^{-6}$; $I^2 = 0\%$; $\tau^2 = 0$; Q test $p = 0.71$). By looking at the prediction intervals, the comparison relative to the “self-blame” subscale became not significant. The single study that included only people in euthymia had a higher effect size than the other in the comparisons relative to the “self-blame” and “catastrophizing” subscales.

Additional information about the main, sensitivity, cumulative, and subgroup analyses is presented in [Supplementary Materials](#) n.1.

3.2.4. Risk-taking behavior

A total of 13 cross-sectional studies including 870 patients diagnosed with BD and 647 HCs explored the extent of risk-taking or impulsive behaviors among these groups. Specifically, 10 studies (Becerra et al., 2016; Carruthers et al., 2022; Das et al., 2014; Linke et al., 2020; Musket et al., 2021; Oh et al., 2019; Oymak Yenilmez et al., 2021; Sağlam et al., 2020; Van Rheenen et al., 2020, 2015) adopted the DERS, and 3 studies (Fletcher et al., 2013; Perich et al., 2011; Van der Gucht et al., 2009) used the RSQ. Five studies (Becerra et al., 2016; Das et al., 2014; Oh

et al., 2019; Oymak Yenilmez et al., 2021; Van Rheenen et al., 2020) included only people in euthymia, and seven studies (Carruthers et al., 2022; Linke et al., 2020; Musket et al., 2021; Perich et al., 2011; Sağlam et al., 2020; Van der Gucht et al., 2009; Van Rheenen et al., 2015) included a majority of euthymic patients together with others who were depressed or manic.

BD patients presented significant higher scores at the “impulse” subscale of the DERS (SMD=1.11; 95% C.I.=0.78, 1.43; $p = 2.93 \times 10^{-11}$; $I^2 = 80.5\%$; $\tau^2 = 0.22$; Q test $p < 0.01$), and at the “risk-taking” subscale of the RSQ (SMD=0.8; 95% C.I.=0.55, 1.06; $p = 1.09 \times 10^{-9}$; $I^2 = 49.9\%$; $\tau^2 = 0.03$; Q test $p = 0.14$). By looking at the prediction intervals, the comparisons remained significant. By conducting sensitivity analyses, removing any of the studies, or considering just good-quality ones did not change the significance and the direction of the comparisons. Subgroup analysis showed that among the studies exploring the differences in the “impulse” subscale studies including only people in euthymia presented a lower effect size than the ones including people in any mood state. In the same comparison, both studies including the highest percentage of depressed (Van Rheenen et al., 2015) or manic (Musket et al., 2021) patients had a higher effect size than those that considered people in euthymia. By inspecting the GOSH plots, subsets including the Linke 2020 study seemed to present higher heterogeneity and effect size in the comparison relative to the “impulse” subscale. There was no evidence of publication bias for the comparison relative to the “impulse” subscale.

A total of 3 cross-sectional studies (Linke et al., 2020; Sağlam et al., 2020; Van Rheenen et al., 2020) including 145 patients diagnosed with BD and 142 unaffected FDRs explored the extent of risk-taking or impulsive behaviors among these groups. One study (Van Rheenen et al., 2020) included only patients in euthymia, while the others included a majority of euthymic patients together with others who were depressed or manic.

BD patients presented significantly higher scores at the “impulse” subscale of the DERS (SMD=1.05; 95% C.I.=0.68, 1.42; $p = 2.9 \times 10^{-8}$; $I^2 = 53.7\%$; $\tau^2 = 0.06$; Q test $p = 0.12$). By looking at the prediction intervals, the comparison remained significant. By conducting sensitivity analyses, removing any of the studies did not change its significance or direction. The single study that included only people in euthymia had a lower effect size than the others who did not. By inspecting the GOSH plots, subsets including the Linke 2020 study seemed to present higher heterogeneity and effect size.

Additional information about the main, sensitivity, cumulative, and subgroup analyses, and the publication bias is presented in [Supplementary Materials](#) n.1.

3.2.5. Suppression

A total of 3 cross-sectional studies (Aslan and Baldwin, 2021; Oh et al., 2019; Zhang et al., 2018) and 1 prospective-cohort study (Johnson

et al., 2016) including 175 patients diagnosed with BD and 170 HCs explored the extent of the suppression among these groups. One study (Oh et al., 2019) included only euthymic patients, one study (Aslan and Baldwin, 2021) included only depressed patients, and one study (Zhang et al., 2018) included both euthymic and depressed patients. The remaining study did not provide detailed information about the mood state of included patients.

BD patients presented significantly higher scores at the “suppression” subscale (SMD=0.29; 95% C.I.=0.02, 0.55; $p = 0.04$; $I^2 = 32.6\%$; $\tau^2 = 0.02$; Q test $p = 0.25$) of the ERQ, but by looking at the prediction intervals, the comparison did not remain significant. By conducting sensitivity analysis, removing any of the studies, except for Johnson 2016, the comparison became not significant. Studies whose sample was totally (Aslan and Baldwin, 2021) or partly (Zhang et al., 2018) depressed had higher effect sizes than the others.

Additional information about the main, sensitivity, and cumulative analyses is presented in [Supplementary Materials n.1](#).

3.2.6. Dampening

A total of 5 cross-sectional studies (Edge et al., 2013; Fletcher et al., 2013; Peckham et al., 2016; Shapero et al., 2015; Weinstock et al., 2018) and 1 prospective-cohort study (Johnson et al., 2016) including 440 patients diagnosed with BD and 506 HCs explored the extent of the dampening among these groups. Two studies (Peckham et al., 2016; Shapero et al., 2015) included only euthymic patients, and one study (Weinstock et al., 2018) included only depressed patients. The remaining studies did not provide detailed information about the mood state of people with BD.

BD patients presented significantly higher scores at the “dampening” subscale of the RPA (SMD=1; 95% C.I.=0.7, 1.31; $p = 1.45e-10$; $I^2 = 73.3\%$; $\tau^2 = 0.1$; Q test $p < 0.01$), and by looking at the prediction intervals, the comparison remained significant. By conducting sensitivity analysis, removing any of the studies from the comparison did not change its significance or direction. Subgroup analysis showed that the studies including only people in euthymia presented a lower effect size than the ones including people in any mood state, and this difference was significant. Besides, the study (Weinstock et al., 2018) including only depressed patients had the highest effect size among those evaluated in the comparison. By inspecting the GOSH plots, subsets including the Shapero 2015 study seemed to present higher heterogeneity and lower effect size.

Additional information about the main, sensitivity, and cumulative analyses is presented in [Supplementary Materials n.1](#).

3.3. Adaptive emotion regulation strategies

3.3.1. Cognitive reframing

A total of 9 cross-sectional, and 1 prospective-cohort studies encompassing 659 patients diagnosed with BD and 490 HCs explored the extent of cognitive reframing among these groups. Specifically, 6 studies (Fletcher et al., 2013; Green et al., 2011; Hassani and Kia, 2016; Kanske et al., 2015; Rowland et al., 2013; Wolkenstein et al., 2014) adopted the CERQ, while 4 studies (Aslan and Baldwin, 2021; Johnson et al., 2016; Oh et al., 2019; Zhang et al., 2018) used the ERQ. Three studies (Kanske et al., 2015; Oh et al., 2019; Wolkenstein et al., 2014) included only euthymic patients, one study (Aslan and Baldwin, 2021) included only depressed patients, and one study (Zhang et al., 2018) included both euthymic and depressed patients. The remaining studies did not provide detailed information about the mood state of included patients.

BD patients presented significantly lower scores at the “putting into perspective” (SMD= -0.67; 95% C.I.= -0.96, -0.37; $p = 1.07e-5$; $I^2 = 71.9\%$; $\tau^2 = 0.09$; Q test $p < 0.01$), “positive refocusing” (SMD= -0.52; 95% C.I.= -0.9, -0.14; $p = 0.01$; $I^2 = 83.2\%$; $\tau^2 = 0.18$; Q test $p < 0.01$), “positive reappraisal” (SMD= -0.6; 95% C.I.= -0.91, -0.29; $p = 1.7e-4$; $I^2 = 75.1\%$; $\tau^2 = 0.11$; Q test $p < 0.01$), and “refocus on planning” subscales of the CERQ (SMD= -0.44; 95% C.I.= -0.79, -0.08; $p = 0.02$; I^2

=81.1%; $\tau^2 = 0.15$; Q test $p < 0.01$), and at the “reappraisal” subscale of the ERQ (SMD= -0.54; 95% C.I.= -0.94, -0.14; $p = 0.01$; $I^2 = 68.2\%$; $\tau^2 = 0.11$; Q test $p = 0.02$). By looking at the prediction intervals, all the comparisons became not significant except for the one relative to the “putting into perspective” subscale. By conducting sensitivity analyses, removing any of the studies did not change the significance and the direction of the comparisons, except for the one relative to the “reappraisal” subscale in which removing the Johnson 2016 study made the overall effect not significant. Considering only good-quality studies, the comparisons remained significant except for the ones relative to “positive reappraisal” and “reappraisal” subscales and presented a lower but more precise effect size. Subgroup analysis showed that among the meta-analyses relative to the “putting into perspective”, “positive refocusing” and “positive reappraisal” subscales, the studies including only people diagnosed with BD-I presented a lower effect size and reduced heterogeneity, while in the comparison relative to the “reappraisal” subscale, the study including only people in euthymia presented a lower and not significant effect size. Studies including only euthymic patients had respectively lower and higher effect sizes state in the comparisons relative to the “putting into perspective” and “positive reappraisal”, and “positive refocusing” and “refocus on planning” subscales than those considering patients in any mood state: still, these differences were not significant. Studies whose sample was totally (Aslan and Baldwin, 2021) or partly (Zhang et al., 2018) depressed had greater effect sizes than the others. By inspecting the GOSH plots, subsets including the Fletcher 2013 study seemed to present in the comparisons relative to “positive refocusing”, “positive reappraisal”, and “refocus on planning” subscales with higher heterogeneity and effect size than those who did not, while subsets including the Oh 2019 study seemed to present higher heterogeneity and lower effect size in the comparison relative to the “reappraisal” subscale.

A total of 2 cross-sectional studies (Green et al., 2011; Kanske et al., 2015) including 127 patients diagnosed with BD and 141 unaffected FDRs explored the extent of cognitive reframing among these groups. One study (Kanske et al., 2015) included only people in euthymia, while the other did not provide detailed information about the mood state of these patients.

BD patients presented significantly lower scores at the “putting into perspective” subscale of the CERQ (SMD= -0.4; 95% C.I.= -0.64, -0.16; $p = 1.3e-3$; $I^2 = 0\%$; $\tau^2 = 0$; Q test $p = 0.72$), and by looking at the prediction intervals the comparison remained significant. The single study that included only people in euthymia had a smaller effect size in the comparison relative to the “putting into perspective” subscale, and a greater one in the comparisons relative to the “positive reappraisal” and “refocus on planning” subscales.

Additional information about the main, sensitivity, cumulative, and subgroup analyses is presented in [Supplementary Materials n.1](#).

3.3.2. Adaptive coping

A total of 13 cross-sectional studies including 870 patients diagnosed with BD and 647 HCs explored the extent of adaptive coping among these groups. Specifically, 10 studies (Becerra et al., 2016; Carruthers et al., 2022; Das et al., 2014; Linke et al., 2020; Musket et al., 2021; Oh et al., 2019; Oymak Yenilmez et al., 2021; Sağlam et al., 2020; Van Rheenen et al., 2020, 2015) adopted the DERS, and 3 studies (Fletcher et al., 2013; Perich et al., 2011; Van der Gucht et al., 2009) used the RSQ. Five studies (Becerra et al., 2016; Das et al., 2014; Oh et al., 2019; Oymak Yenilmez et al., 2021; Van Rheenen et al., 2020) included only people in euthymia, and seven studies (Carruthers et al., 2022; Linke et al., 2020; Musket et al., 2021; Perich et al., 2011; Sağlam et al., 2020; Van der Gucht et al., 2009; Van Rheenen et al., 2015) included a majority of euthymic patients together with others who were depressed or manic.

BD patients presented significantly higher scores at the “goals” (SMD=0.94; 95% C.I.=0.65, 1.22; $p = 1.32e-10$; $I^2 = 75.4\%$; $\tau^2 = 0.15$; Q test $p < 0.01$), and “strategies” subscales of the DERS (SMD=1.27; 95%

C.I.=0.96, 1.59; $p = 1.93\text{e-}15$; $I^2 = 78.1\%$; $\tau^2 = 0.19$; Q test $p < 0.01$), and lower scores at the “adaptive” subscale of the RSQ (SMD= -0.82; 95% C.I.= -1.38, -0.25; $p = 4.5\text{e-}3$; $I^2 = 89.3\%$; $\tau^2 = 0.22$; Q test $p < 0.01$). By looking at the prediction intervals, these comparisons remained significant except for the “adaptive” subscale. By conducting sensitivity analyses, the removal of any of the studies did not change the significance and the direction of the comparisons, except for the “adaptive” subscale, in which, after the removal of the Perich 2011 study, the overall effect became not significant. Considering only good-quality studies, the comparisons remained significant except for the one relative to the “adaptive” subscale and presented a lower effect size. Subgroup analysis showed that among the studies relative to the “goals” subscale, those including only people in euthymia presented a lower effect size and reduced heterogeneity. The same was observed when considering the “strategies” subscale, although this difference was not significant. In both comparisons, studies including the highest percentage of depressed (Van Rheenen et al., 2015) or manic (Musket et al., 2021) patients had a higher effect size than those that considered people in euthymia. By inspecting the GOSH plots, subsets including the Linke 2020 study seemed to present higher heterogeneity and effect size in the comparison relative to the “goals” and “strategies” subscales, while subsets including the Oh 2019 study seemed to present higher heterogeneity and lower effects size in the comparison relative to the “strategies” subscale. There was no evidence of publication bias for the comparison relative to the “goals” and “strategies” subscales.

A total of 3 cross-sectional studies (Linke et al., 2020; Sağlam et al., 2020; Van Rheenen et al., 2020) including 145 patients diagnosed with BD and 142 unaffected FDRs explored the extent of adaptive coping among these groups. One study (Van Rheenen et al., 2020) included only patients in euthymia, while the others included a majority of euthymic patients together with others who were depressed or manic.

BD patients presented significantly higher scores at the “goals” (SMD=0.69; 95% C.I.=0.4, 0.98; $p = 2.9\text{e-}6$; $I^2 = 30.6\%$; $\tau^2 = 0.02$; Q test $p = 0.25$) and “strategies” subscales of the DERS (SMD=1.04; 95% C.I.=0.63, 1.44; $p = 4.5\text{e-}7$; $I^2 = 60.9\%$; $\tau^2 = 0.08$; Q test $p = 0.09$). By looking at the prediction intervals, all these comparisons remained significant. By conducting sensitivity analyses, removing any of the studies did not change the significance and the direction of the comparisons. The single study that included only people in euthymia had a lower effect size than the others who did not, and it was not significant in the comparison relative to the “goals” subscale.

Additional information about the main, sensitivity, cumulative, and subgroup analyses, and the publication bias is presented in [Supplementary Materials n.1](#).

3.3.3. Acceptance

A total of 16 cross-sectional studies including 964 patients diagnosed with BD and 770 HCs explored the extent of acceptance among these groups. Specifically, 10 studies (Becerra et al., 2016; Carruthers et al., 2022; Das et al., 2014; Linke et al., 2020; Musket et al., 2021; Oh et al., 2019; Oymak Yenilmez et al., 2021; Sağlam et al., 2020; Van Rheenen et al., 2020, 2015) adopted the DERS, while 6 studies (Fletcher et al., 2013; Green et al., 2011; Hassani and Kia, 2016; Kanske et al., 2015; Rowland et al., 2013; Wolkenstein et al., 2014) used the CERQ. Seven studies (Becerra et al., 2016; Das et al., 2014; Kanske et al., 2015; Oh et al., 2019; Oymak Yenilmez et al., 2021; Van Rheenen et al., 2020; Wolkenstein et al., 2014) included people in euthymia, and five studies (Carruthers et al., 2022; Linke et al., 2020; Musket et al., 2021; Sağlam et al., 2020; Van Rheenen et al., 2015) included a majority of euthymic patients together with others who were depressed or manic. The remaining studies did not provide detailed information about the mood state of included patients.

BD patients presented significant higher scores at the “acceptance” subscale of the CERQ (SMD=0.16; 95% C.I.=0.02, 0.31; $p = 0.02$; $I^2 = 0\%$; $\tau^2 = 0$; Q test $p = 0.74$), and at the “non acceptance” (SMD=0.84; 95% C.I.=0.59, 1.1; $p = 5.57\text{e-}11$; $I^2 = 69\%$; $\tau^2 = 0.11$; Q test $p < 0.01$),

and “clarity” subscales of the DERS (SMD=0.59; 95% C.I.=0.34, 0.83; $p = 4.1\text{e-}6$; $I^2 = 69.4\%$; $\tau^2 = 0.11$; Q test $p < 0.01$). By looking at the prediction intervals, all these comparisons remained significant except for the one relative to the “clarity” subscale. By conducting sensitivity analyses, removing any of the studies did not change the significance and the direction of the comparisons, except for the one relative to the “awareness” subscale in which, by removing Becerra 2016, the overall effect became significant, and to the “acceptance” subscale in which, by removing Fletcher 2013 or Rowland 2013”, the overall effect became not significant. Considering only good-quality studies, the comparisons relative to the “acceptance” and “clarity” subscales became not significant. Subgroup analysis showed that among the studies relative to the “clarity” subscale, those including only people diagnosed with BD-I presented a significantly lower effect size and reduced heterogeneity than the ones including people diagnosed with any type of BD.

Single studies including only euthymic patients presented lower effect sizes in all these comparisons, and the subgroups significantly differed when looking at the “strategies” subscale. The studies including the highest percentage of depressed (Van Rheenen et al., 2015) patients had a higher effect size in the comparisons relative to “non acceptance” and “strategies” subscales. On the contrary it did not differ in terms of effect size in the comparison relative to the “awareness” subscale. By inspecting the GOSH plots, subsets including the Linke 2020 study seemed to present higher heterogeneity and effect size in the comparisons relative to the “non acceptance” and “awareness” subscales; subsets including the Oh 2019 and Becerra 2016 studies seemed to present higher heterogeneity and lower effects size in the comparisons relative to the “clarity”, and “awareness” subscales, respectively. There was no evidence of publication bias for the comparison relative to the “non acceptance” and “clarity” subscales.

A total of 5 cross-sectional studies (Green et al., 2011; Kanske et al., 2015; Linke et al., 2020; Sağlam et al., 2020; Van Rheenen et al., 2020) including 272 patients diagnosed with BD and 283 unaffected FDRs explored the extent of acceptance among these groups. Two studies (Kanske et al., 2015; Van Rheenen et al., 2020) included only patients in euthymia, and two studies (Linke et al., 2020; Sağlam et al., 2020) included a majority of euthymic patients together with others who were depressed or manic. The remaining study did not provide detailed information about the mood state of included patients.

BD patients presented significantly higher scores at the “non acceptance” (SMD=0.74; 95% C.I.=0.36, 1.12; $p = 1.3\text{e-}4$; $I^2 = 58.3\%$; $\tau^2 = 0.07$; Q test $p = 0.1$), and “clarity” subscales of the DERS (SMD=0.5; 95% C.I.=0.24, 0.76; $p = 1.3\text{e-}4$; $I^2 = 14.8\%$; $\tau^2 = 0.01$; Q test $p = 0.34$). By looking at the prediction intervals, all these comparisons remained significant. By conducting sensitivity analyses, removing any of the studies did not change the significance and the direction of the comparisons. The study (Van Rheenen et al., 2020) that included only people in euthymia had lower effect sizes in both comparisons than the others who did not. By inspecting the GOSH plots, subsets including the Linke 2020 study seemed to present higher heterogeneity and effect size in the comparison relative to the “non acceptance” subscale, while subsets including the Van Rheenen 2020 study seemed to present higher heterogeneity and lower effects size in the comparison relative to the “awareness” subscale.

Additional information about the main, sensitivity, cumulative, and subgroup analyses, and the publication bias is presented in [Supplementary Materials n.1](#).

4. Discussion

The present systematic review and meta-analysis aimed at describing which ER strategies and ED features are typical of people diagnosed with BD in comparison to non-clinical populations. BD patients adopt more maladaptive ER strategies when compared to HCs. This difference is maintained when compared to unaffected FDRs, even if it appears to be lower.

Specifically, people diagnosed with BD display limited access to ER strategies and an excessive focus on negative aspects of life events when compared to HCs, anticipating catastrophic consequences, and accusing themselves or others of things that happen to them. As suggested by another study focusing on the same population (Nitzburg et al., 2016), the problems experienced by these patients in the early phases of the illness can lead to negative experiences, which may trigger discouragement and self-criticism. In turn, self-blame appears to be associated with lower real-world functioning, resulting in a worsening of BD.

Rumination is a form of thinking concerning excessive and constant thoughts that prevent other forms of mental activity, and a higher likelihood to ruminate was observed in BD. This finding is important considering the role that rumination may have on the onset of dysregulated behaviors or poor sleep quality (Watkins and Roberts, 2020), possibly leading to a worsening of the course of illness (Alloy et al., 2017). Moreover, rumination interferes with concentration, problem-solving or goal-directed activities (Watkins and Roberts, 2020), which is consistent with the higher scores obtained in specific subscales of the DERS.

People diagnosed with BD presented greater risky or impulsive behaviors in response to negative emotions that are experienced as overwhelming and out of control. This appears to be in line with existing literature aimed at exploring this relationship through neurocognitive tests (Ramírez-Martín et al., 2020). Indeed, trait impulsivity is common in individuals with BD and affective patients within the BD spectrum (Furio et al., 2021), and it is associated with poorer clinical outcomes (Etain et al., 2013) and higher suicide risk (Jiménez et al., 2016). Although these aspects appear to be common to all BD patients, the affective state may influence them. In fact, the high impulsivity observed in euthymic individuals appears to be even more pronounced in samples with a higher proportion of depressed and manic patients, even though it may stand on different theoretical grounds. Impulsive behavior in the manic patient may be driven by motor-like impulsivity combined with an inability to delay a reward-related response. On the other hand, in the depressed patient it may occur as an attentional or no-planning impulsivity that seems to be related to hopelessness and anhedonia (Swann et al., 2008).

Suppression is a maladaptive ER strategy that involves the inhibition of ongoing emotion-expressive behavior. We found that people with BD were more likely to adopt this strategy. A possible explanation of this phenomenon might be the presence of alterations in several brain areas, such as the prefrontal cortex and amygdala, that were also associated with expressive suppression in neuroimaging studies (Cutuli, 2014). Depressive symptoms may also play an important role and our review found that depressed patients made greater use of this ER strategy. Cognitive deficits are often associated with depression (Richardson and Adams, 2018) and may make it difficult to employ some adaptive ER strategies, facilitating the use of suppression as an alternative way to ward off an unpleasant emotional state (Dryman and Heimberg, 2018). However, due to the small effect size of the comparison and the wideness of the prediction intervals, more studies are needed to clarify to which extent BD patients differ from HCs in containing their feelings.

When looking at the adaptive ER strategies, an opposite trend emerges. Nonetheless, the fact that people with BD are less likely to positively reframe an experience or be able to distract themselves by initiating amusing activities should be taken with caution, since the prediction intervals crossed the null value in most of these results. Similarly, the extent to which these populations differ in terms of acceptance of experienced negative emotions is controversial. Mood state may partly explain this issue since our results showed that depressed BD patients felt more embarrassed, angry, guilty, ashamed, or irritated when they got upset. However, in our review we did not find studies specifically conducted on depressed patients addressing the acceptance, which limits our observations on this topic.

Retrieved evidence suggests that BD patients are more prone to calm down their own positive emotions than to amplify them. BD strongly

impacts patients' and their families' lives, leaving them with feelings of guilt, shame, or regret the things that may happen during an acute mood episode (Granek et al., 2016), and numbing positive feelings could be interpreted as a personal strategy to cope with manic or hypomanic symptomatology (Edge et al., 2013). Probably for the same reason, studies including only people diagnosed with BD-I presented a greater effect size in this comparison, and among the others, the lowest effect was carried by the study which included the smallest percentage of patients with BD-I (Shapero et al., 2015). Interestingly, the study that included only depressed patients had the highest effect size, and the reason may have to be found in the scale used to measure this aspect. Actually, some of the items (Feldman et al., 2008) that form the "dampening" subscale of the RPA recall negative and catastrophic thoughts, so patients with lower mood may be more prone to give higher scores to these specific items.

People diagnosed with BD-I employed more adaptive and fewer maladaptive ER strategies than those diagnosed with any BD type. This is possibly related to the chronic clinical course of BD-II with shorter interval episodes, higher comorbidity rates, and less defined treatment strategies (Berk and Dodd, 2005; Vieta, 2019), which could be responsible for partial management of syndromic and subsyndromal symptoms.

BD patients experiencing euthymia had lower levels of ED than patients in any mood state, suggesting that ED in BD might be a trait feature enhanced by the current mood state. This appears to be in contrast with existing research conducted on different clinical populations (i.e., anorexia nervosa), in which ED seems to be more a state than a trait feature (Harrison et al., 2010b). However, these results were based on a sample of patients with very low self-reported depression that could have biased ED self-reports, considering the relationship between ED and depressive symptoms (Harrison et al., 2010a). Indeed, another study conducted on the same clinical population failed to find a reduction of ED levels sufficient to match those of the HCs, despite the clinical improvement observed (Cassioli et al., 2022). The high prevalence of persisting depressive subsyndromal symptoms in people with BD (Grunze and Born, 2020) could help us to explain the persistence of moderate-to-high effect sizes observed even among the patients in euthymia. The relationship between overall ED and manic symptomatology remains unclear. Only a few papers have provided us with detailed information regarding this association, and the study that included the highest proportion of manic patients had a low effect size. Different and contrasting results are available in existing literature with generally modest correlations (Fletcher et al., 2019; Khosravani et al., 2021), so that additional research on the topic is required.

Unfortunately, due to the paucity of data on the matter, the role of psychiatric comorbidities on the magnitude of the effects could not be sorted out, although it seems that they could drive it towards higher values. For example, the Linke 2020 study, which appeared to be a visible outlier in many comparisons regarding the DERS, included plenty of patients who were comorbid with attention deficit hyperactivity disorder (ADHD) or anxiety disorders, displaying the highest difference with HCs. ADHD (Faraone et al., 2019) and anxiety disorders (Sackl-Pammer et al., 2019) are deeply related to ED, and comorbid samples could be overloaded with an additional burden on their psychopathology.

Due to the extent of cyclothymic temperamental traits in patients diagnosed with BD (Morishita et al., 2021), or the high prevalence of comorbid borderline personality disorder (Fornaro et al., 2016), it is also possible to expect that at least a portion of the samples included in our meta-analysis may present these characteristics. This should be taken into consideration, since more prominent cyclothymic temperaments are often related to higher levels of ED (Taş and Altınbaş, 2020), and people with BD and comorbid borderline personality disorder may present more difficulties in ER than not comorbid people (Bayes et al., 2016). However, two of the included studies (Perich et al., 2011; Wolkenstein et al., 2014) still presented comparisons with moderate-to-high

effect sizes, despite having specifically excluded from their sample people diagnosed with personality disorders, suggesting that other features should be considered to untangle this complex construct.

When compared to unaffected FDRs, people with BD continued to exhibit a scanner range of ER strategies and also a higher propensity to ruminate or catastrophize. Still, many of the comparisons relative to the adaptive ER strategies failed to show a significant difference. All these observations presented a lower effect size than the ones related to BD-HCs comparisons, supporting the idea that FDRs, even if unaffected, constitute a population at higher risk for BD (Birmaher et al., 2022; Kupka et al., 2021), and difficulties in ER could represent the starting point or at least a measurable correlate of broader, syndromic psychopathological issues. Indeed, ED seems to spread on a continuum: a dilution of these features occurs from BDs to HCs, and unaffected FDRs lie somewhere in between on this gradient. However, due to the few included studies exploring these comparisons, additional investigation is needed on the matter.

The present systematic review and meta-analysis included only those studies that adopted self-report measures to assess the regular use of specific ER strategies. However, although these instruments are the most widely used in the literature on the topic, they appear to be conditioned by the subject's memory and willingness to respond, and often do not consider the natural context in which the ER strategy is likely to be implemented. Ecological momentary assessments (EMA) through daily diaries or experience sampling methods (ESM), are useful techniques for measuring the complexity of the ER in its natural environment by longitudinally assessing these strategies over several days (Boemo et al., 2022). Studies specifically focused on people diagnosed with BD and adopting these designs showed that specific ER strategies like rumination and risk-taking behaviors were associated with lower self-esteem and higher negative (Leung et al., 2019; Pavlickova et al., 2013) and positive affect (Pavlickova et al., 2013) at a subsequent time-point, respectively. The same holds true in reverse, and the presence of negative or positive affect at a specific time-point appears to predict the implementation of one of these ER strategies at a later moment (Leung et al., 2019; Pavlickova et al., 2013). The ESM was also used to analyze the inter-relationships between mood and ER strategies in a young population of FDR of people diagnosed with BD (Pavlickova et al., 2015), and the results were similar to those observed in clinical populations, albeit with lower effect sizes. Although our work could not take into account the complex interactions assessed by these types of studies, our results appear consistent with them and highlight the role of ER strategies, such as rumination or risk-taking behavior, in BD.

To the best of our knowledge, this is the first systematic review and meta-analysis which focuses on multiple aspects of ED in people diagnosed with BD, since previous reviews on the matter did not attempt a quantitative approach (Dodd et al., 2019) or were limited to specific aspects of this association (Kovács et al., 2020; Miola et al., 2022). Although ED remains a complex and multifaceted construct that is difficult to characterize precisely, our results help define its clinical presentation in BD, characterized mostly by increased adoption of maladaptive ER strategies, like rumination or risk-taking behavior, rather than a reduced adoption of the adaptive ones. This, along with the minor differences found when comparing with unaffected FDRs, has important clinical and research implications. From a clinical perspective, ED could be targeted by prevention programs to reduce the psychopathological burden in individuals with an increased risk of BD (i.e., FDRs) (Sugranyes and Serna, 2021). Also, psychological interventions in BD should integrate the enhancement of ER strategies to improve the clinical outcome of patients with BD. From a research perspective, a clearer understanding of ED in BD could refine future research into the biological, psychological, and environmental factors that influence this disorder, allowing for ED-specific psychological and pharmacological interventions. Because of its relationship with alterations in the amygdala, prefrontal cortex, and their connections, ED should be also explored to better define its role in BD neuroprogression (Serafini et al.,

2021), advancing the hypothesis that higher levels of ED may be associated with greater neuroprogression, and may explain at least in part the treatment resistance described therein (Bauer et al., 2017). Furthermore, more studies including unaffected FDRs should be conducted to investigate the hypothesis that this population may stand on a clinical and neurobiological continuum towards the full threshold BD.

The present study has some limitations. First, due to the insufficiency of the number of studies included, it was not possible to perform meta-regressions to study the impact of continuous variables (i.e., mean age, percentage of females among the populations, percentage of people in a particular mood state) on the overall effect size. Second, many of the explored differences were large but this may be due to the use of self-report measures. Even if the present review focused on those instruments because of their clinical relevance, lower effect sizes when exploring the topic with hetero-reported assessment could be reasonably expected. Third, sample sizes differed much across the comparisons and were small in general, suggesting the need to further studies on the matter.

5. Conclusions

People diagnosed with bipolar disorder present high levels of emotion dysregulation that impact the overall functioning and quality of life. Among the maladaptive regulation strategies, negative focus, rumination, and risk-taking behaviors are the most frequent, whilst the evidence relative to the adaptive strategies is unclear. First-degree relatives present similar alterations compared to fully syndromic individuals, suggesting that emotion dysregulations could be partly heritable, but further research on the topic extended to broader populations is required.

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Declaration of interest

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Data Availability

The datasets and the codes used for this research are fully available on request.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.neubiorev.2022.104914.

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