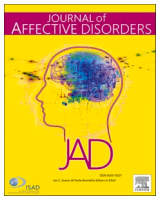
Journal of Affective Disorders 394 (2026) 120605

Contents lists available at ScienceDirect

Journal of Affective Disorders

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



Review Article

Neural signatures of bipolar disorder subtypes: A comprehensive systematic review of neuroimaging studies

Alessandro Miola [a,b,c,1], Margherita Salvucci [a,1,2], Nicola Meda [a,b], Giulia Cattarinussi [d], Maria Lavinia Loré [a], Niccolò Ghiotto [a], Enrico Collantoni [a,b], Tommaso Boldrini [e,m], Nicolas A. Nunez [c,f], Mete Ercis [c], Michele De Prisco [g,h,i,j], Michele Fornaro [k], Marco Solmi [l,m,n,o,p], Marin Veldic [c], Joaquim Radua [h,i,j], Eduard Vieta [g,h,i,j], Mark A. Frye [c], Fabio Sambataro [a,b,*]

[a] Department of Neuroscience (DNS), University of Padova, Padua, Italy
[b] Padua Neuroscience Center, University of Padova, Padua, Italy
[c] Department of Psychiatry and Psychology, Mayo Clinic, Rochester, MN, USA
[d] Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
[e] Department of Psychology and Educational Science, Pegaso Telematic University, Naples, Italy
[f] Department of Psychiatry, University of Utah, Salt Lake City, UT, USA
[g] Bipolar and Depressive Disorders Unit, Hospital Clinic de Barcelona, Barcelona, Spain
[h] Institut d'Investigacions Biomediques August Pi i Sunyer (IDIBAPS), University of Barcelona, Barcelona, Spain
[i] Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Instituto de Salud Carlos III, Madrid, Spain
[j] Department of Medicine, Faculty of Medicine and Health Sciences, Institute of Neurosciences (UBNeuro), University of Barcelona (UB), Barcelona, Spain
[k] Department of Psychiatry, Federico II University of Naples, Naples, Italy
[l] SCIENCES lab, Department of Psychiatry, University of Ottawa, Ottawa, ON, Canada
[m] Department of Mental Health, The Ottawa Hospital, Ottawa, ON, Canada
[n] Ottawa Hospital Research Institute (OHRI) Clinical Epidemiology Program, University of Ottawa, Ottawa, ON, Canada
[o] School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada
[p] Department of Child and Adolescent Psychiatry, Charité Universitätsmedizin, Berlin, Germany

ARTICLE INFO

Keywords:
Bipolar disorder
Bipolar subtypes
Neuroimaging
Emotion regulation
Systematic review

ABSTRACT

The neurobiological mechanisms differentiating bipolar disorder type I (BD-I) from type II (BD-II) remain poorly understood. A comprehensive synthesis systematically comparing neuroimaging findings between BD subtypes is lacking. We conducted a systematic review (PubMed, Scopus, up to March 2024), including structural MRI, functional MRI, and diffusion tensor imaging studies, to provide a comprehensive overview of the common and distinct candidate neural signatures that differentiate BD subtypes. Out of the initial 5334 references, 38 MRI studies (41 experiments) were included. Structural MRI studies showed mixed results regarding volumetric and cortical surface differences between BD subtypes. BD-I exhibited widespread gray matter (GM) volume reductions, larger lateral ventricles, and decreases in cortical thickness. Hippocampal and cerebellar volume reductions were observed in both BD subtypes but did not differentiate BD-I from BD-II. While white matter (WM) abnormalities across BD subtypes remain heterogeneous and lack consistent replication, BD-I showed a tendency toward more disrupted WM microstructure and higher WM hyperintensities rates than BD-II. Functional MRI studies revealed distinct differences in task-based and resting-state activity, suggesting differential neural patterns in reward processing and emotion regulation. BD-I displayed a greater disconnection in emotion regulation circuits. While both BD-I and BD-II share some neuroimaging characteristics, the findings suggest BD-I is characterized by more pronounced WM disruptions and emotion dysregulation. In contrast, BD-II shows more remarkable subcortical volume preservation but with distinct connectivity alterations. These results offer insights into the different and shared neurobiological mechanisms of BD subtypes, which may help refine their pathophysiology and inform tailored interventions.

* Corresponding author at: Department of Neuroscience (DNS), University of Padova, via Belzoni 160, I-35121, Padua, Italy.
E-mail address: fabio.sambataro@unipd.it (F. Sambataro).
[1] These authors contributed equally to this work.
[2] Deceased.

https://doi.org/10.1016/j.jad.2025.120605
Received 5 July 2025; Received in revised form 21 October 2025; Accepted 1 November 2025
Available online 4 November 2025

1. Introduction

Bipolar disorder (BD) is a severe chronic mental illness characterized by recurrent episodes of changes in mood, irritability, energy levels, behavior, and emotional dysregulation (Vieta et al., 2018; Miola et al., 2022a; De Prisco et al., 2023; Oliva et al., 2024). BD type I (BD-I) and BD type II (BD-II) represent the two main subtypes (APA, 2022). BD-I is defined by the occurrence of at least one manic episode, which often manifests as elevated mood, irritability, grandiosity, and increased energy. In contrast, BD-II is characterized by recurrent depressive and hypomanic episodes, which are less severe than full-blown manic episodes (APA, 2022). Differences between BD-I and BD-II are not limited to the severity of (hypo)manic syndromes, as the BD types differ substantially in several descriptive and clinical measures, and the clinical manifestations of BD-II tend to remain diagnostically stable over many years (Hernandorena et al., 2023). Depressive episodes are more prominent and long-lasting in people with BD-II compared to those with BD-I (Tondo et al., 2022). Furthermore, people with BD-II usually present a higher socio-economic status and better cognition and functioning in daily life than those diagnosed as BD-I, despite often greater long-term morbidity as a proportion of time ill (Tondo et al., 2022; Bora, 2025). Indeed, the course of BD-II is typically characterized by depressive onset, early depressive episodes, and depressive predominant polarity, with higher rates of rapid cycling course of illness (Brancati et al., 2023; Miola et al., 2023a, 2023b).

Debates persist regarding the optimal approach to interpret the heterogeneous clinical manifestations within the broad concept of BD. Some authors favor a dichotomous model of hypomanic and manic syndromes (Parker et al., 2016, 2020; Vieta, 2019; Tondo et al., 2022), while others raise concerns about the validity of the BD-I vs. BD-II dichotomy based on the uncertain distinction of hypomania vs. mania and lack of clear boundaries between the two conditions (Malhi et al., 2019; Gitlin and Malhi, 2020).

Neurobiological alterations in BD-I vs *BD-II*. Since the disease expression of BD follows a multifactorial model, with a strong environmental component and the involvement of both rare and common genetic variants (Almeida et al., 2020), a few studies investigated the genetics of the BD spectrum. The polygenic risk load for BD and schizophrenia (SCZ) appears greater in BD-I than in BD-II, which is more strongly genetically correlated with major depressive disorder (MDD), suggesting a different genetic structure of BD subtypes (Charney et al., 2017; O'Connell et al., 2025). Although the genetic basis of BD-I and BD-II is not entirely clarified, there is growing evidence of genetic heterogeneity between the BD subtypes (Richards et al., 2022). Nonetheless, the precise neurobiological mechanisms that differentiate BD-I from BD-II remain a subject of ongoing research.

Neuroimaging measures. Neuroimaging has emerged as a valuable tool for investigating the neural substrates of psychiatric disorders. Voxel-based morphometry (VBM) and surface-based morphometry (SBM) are the methods commonly used to calculate indices of cortical morphology, mainly using T1-weighted magnetic resonance imaging (MRI) (Goto et al., 2022). While VBM is used primarily to estimate gray matter (GM) volume, including that of the cortex, SBM metrics encompass a range of quantitative measures that capture the morphological properties of the brain's cortical surface. These measures include cortical thickness (the distance between the pial surface and the gray-white matter boundary), the cortical surface area (the total area of the surface encompassing a brain region), sulcal depth (the mean distance from the cortical surface of adjoining gyri to the deepest point in the sulcus) and gyrification (the ratio of the total to outer cortical contour allows to estimate the degree of cortical folding) (Zilles et al., 1988; Libero et al., 2014; Jin et al., 2018).

Additionally, diffusion tensor imaging (DTI) is another neuroimaging technique commonly used to study the microstructural organization of white matter (WM) in the brain. Several DTI-based metrics, such as fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD), offer insights into WM integrity by measuring the diffusion of water molecules within the WM tracts (Alexander et al., 2007; Benedetti et al., 2011). Functional magnetic resonance imaging (fMRI) is a non-invasive technique for studying the functioning human brain. fMRI utilizes blood oxygen level-dependent (BOLD) sensitivity methods and allows the study of the function of the brain at rest (rs-fMRI) or during the performance of a specific task (Kotoula et al., 2023). rs-fMRI can measure intrinsic activity and connectivity patterns of the brain. Among whole-brain approaches, seed-based functional connectivity analysis, independent component analysis (ICA), and graph theory-based network analysis are commonly used to study large-scale brain networks and their interactions. Meanwhile, regional approaches, including the amplitude of low-frequency fluctuations (ALFF), the dynamic fractional amplitude of low-frequency fluctuations (d-fALFF), and regional homogeneity (ReHo) analysis, focus on local neural dynamics and synchronization within specific brain regions (Zou et al., 2008; Smitha et al., 2017). Task-based fMRI enables the assessment of brain activation and connectivity by measuring changes in blood flow and oxygen levels associated with neuronal activity. This technique helps identify brain regions activated in response to a specific task, providing insights into brain segregation. On the other hand, by evaluating functional connectivity, task-based fMRI offers a comprehensive understanding of how neural networks are integrated to support complex processes (Gerchen and Kirsch, 2017; Al-Arfaj et al., 2023).

Neuroimaging changes in BD. Previous literature suggests alterations in structural and functional neuroimaging in BD compared with healthy controls (HC). A previous multimodal meta-analysis showed that people with BD present similar aberrant brain activity and structure patterns in regions encompassing the insula extending to the temporal cortex, frontal-striatal-thalamic, and default-mode network (Chen et al., 2022). Moreover, large-scale studies by the worldwide ENIGMA consortium revealed cortical abnormalities, with individuals with BD presenting a thinner cortex in both hemispheres' frontal, temporal, and parietal regions (Hibar et al., 2018). Other studies found differences in subcortical regional volumes, with people with BD showing a reduced volume in the hippocampus and thalamus and wider lateral ventricles (Hibar et al., 2016). A recent systematic review of 14 MRI studies supports an altered and heterogeneous brain gyrification pattern in individuals with BD, spanning large anatomical and functional neural networks associated with processing and affective regulation difficulties, altered cognitive functioning, and clinical symptoms (Miola et al., 2022b). Moreover, DTI studies revealed a decreased mean FA in people with BD compared to HC; this difference was more evident in the corpus callosum and cingulum and underscored an altered WM integrity and connectivity in BD (Favre et al., 2019). Another recent systematic review and meta-analysis found that BD patients have a higher burden of WM hyperintensities (WMHs) than HC [46.5 % vs 28 %, respectively (pooled Odds Ratio 2.89, 95 % CI 1.76; 4.75)], mostly involving frontal and fronto-parietal regions (Silva et al., 2024).

Interestingly, functional neuroimaging studies reported abnormal brain activity in BD in resting-state and task-based MRI. Studies on resting-state functional connectivity (FC) showed a large-scale network dysfunction in the acute phase compared to the remitted state of BD, with BD patients presenting decreased connectivity within the affective network and the default-mode network during mood episodes (Wang et al., 2020). Task-based functional neuroimaging studies found altered activity in the left amygdala during emotional experiments and in the left superior and right inferior parietal lobules, with increased activity in the left medial orbitofrontal cortex during cognitive tasks (Schumer et al., 2023). Lastly, a recent meta-analysis showed hyperactivation in the ventromedial prefrontal cortex and subgenual anterior cingulate cortex during working memory and increased activity in the orbitofrontal cortex during reward processing in BD compared to HC (Mesbah et al., 2023).

In recent years, neuroimaging studies have played an important role

in unraveling the neural correlates of BD subtypes, offering insights into the potential structural, functional, and connectivity differences that contribute to their clinical presentations. However, there has been no comprehensive synthesis of the existing neuroimaging literature that systematically compares BD-I and BD-II.

This systematic review aims to bridge this gap by systematically examining the neuroimaging studies that have investigated the differences between BD-I and BD-II. By synthesizing findings from diverse neuroimaging approaches, including structural, functional, and diffusion tensor imaging, we aimed to provide a comprehensive overview of the common and candidate neural signatures that differentiate these two BD subtypes.

2. Methods

2.1. Protocol and search strategy

This systematic review followed a pre-defined protocol available online (https://osf.io/dsx57). It adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement (Page et al., 2021) to ensure a high reporting standard. A comprehensive literature search was conducted to identify peer-reviewed articles investigating neuroimaging differences between BD-I and BD-II. The search was performed across two databases (PubMed and Scopus) without any language restriction, from inception to March 21, 2024, using the following search strategy: "(Bipolar disorder OR BD OR bipolar disorder type I OR bipolar disorder type II OR BD-I OR BD-II) AND (sMRI OR structural magnetic resonance imaging OR VBM OR voxel-based morphometry OR SBM OR surface-based morphometry OR cortical thickness OR gyrification OR GI OR sulcal depth OR fractal dimension OR FD OR DTI OR diffusion tensor imaging OR white matter abnormalities OR tract-based spatial statistics OR TBSS OR white matter hyperintensities OR WMH OR functional MRI OR fMRI OR functional neuroimaging)." We also manually searched the reference lists of identified studies.

2.2. Eligibility criteria and study selection

Studies were considered eligible for inclusion if they met the following criteria: (1) included adult participants diagnosed with BD according to standardized diagnostic criteria, including the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD), (2) provided data for the comparison of neuroimaging measures to identify shared and/or distinct differences between BD-subtypes (BD-I vs. BD-II), (3) utilized structural MRI, fMRI, and DTI techniques. Commentaries, case reports, editorials, letters to the editors, and reviews were excluded.

2.3. Data extraction and synthesis

Authors independently conducted the initial screening of titles and abstracts to identify potentially relevant studies (M.S., M.L.L., N.G.). Full texts of selected articles were then retrieved and assessed for eligibility based on the inclusion criteria. Any discrepancies in study selection were resolved through discussion with another author (A.M.) until consensus was reached.

Data extraction was performed using a predefined standardized spreadsheet, including study characteristics (e.g., authors, publication year, study design), participant demographics (e.g., sample size, age, sex distribution), diagnostic criteria, details of the neuroimaging technique (s) utilized (e.g., structural MRI, fMRI, DTI), and neuroimaging findings (e.g., structural differences, FC patterns) related to shared and/or distinct differences between BD-I and BD-II groups.

2.4. Quality assessment

The methodological quality and risk of bias of included studies were assessed independently by the researchers (M.L.L., N.G., A.M., N.M.) with the Imaging Methodology Quality Assessment Checklist (adapted from Strakowski et al., 2000) on the following parameters: subjects, imaging acquisition and analysis, results, and conclusions. Any persisting disagreements on the quality assessment of the included studies were resolved through discussion and consensus.

2.5. Data synthesis and analysis

Due to the expected heterogeneity of methodologies and findings, a narrative synthesis approach was chosen for this systematic review. Extracted data were summarized and categorized according to different neuroimaging modalities (e.g., structural MRI, fMRI, and DTI), highlighting the reported differences between BD-I and BD-II. Emerging themes and patterns from the included studies were discussed to offer insights into the shared neurobiological underpinnings and differences between the two BD subtypes. The spatial distribution of the MRI study findings of structural, functional imaging, and WM tracts was displayed in the whole brain with the *ggplot* package in R.

3. Results

A total of 5334 studies were identified from PubMed and Scopus databases. After duplicate removal, 3907 abstracts were selected, of which 48 articles were retrieved for full-text assessment. Twelve studies were excluded after full-text evaluations, and the reasons for exclusion are reported in Fig. 1. A total of 36 studies, plus two additional reports found in the reference lists of screened reports, were included (Table 1). Overall, this review included 38 MRI studies and 41 experiments. Of these, five were fMRI studies (three rs-fMRI studies and two task-based fMRI investigations, one of which was a multimodal study that included FA analysis). At the same time, the remaining 33 were structural MRI studies. Among the structural MRI investigations, nine assessed WM microstructural abnormalities, three explored WMHs, and the others conducted voxel-based or surface-based analyses of GM alterations. Participant eligibility criteria, including medical and psychiatric comorbidities and medication status, are detailed in Supplementary material (Section 1, eTable 3).

Most studies ($n = 14$) were conducted in Western Europe, nine in Southeast Asia, eight in the United States, two in Australia, and one in Japan; four were international multisite studies. The characteristics of the included studies and their neuroimaging findings are summarized in Tables 1, 2, and 3.

Structural and functional MRI findings are summarized in Fig. 2, and WM tract findings are shown in Fig. 3, respectively.

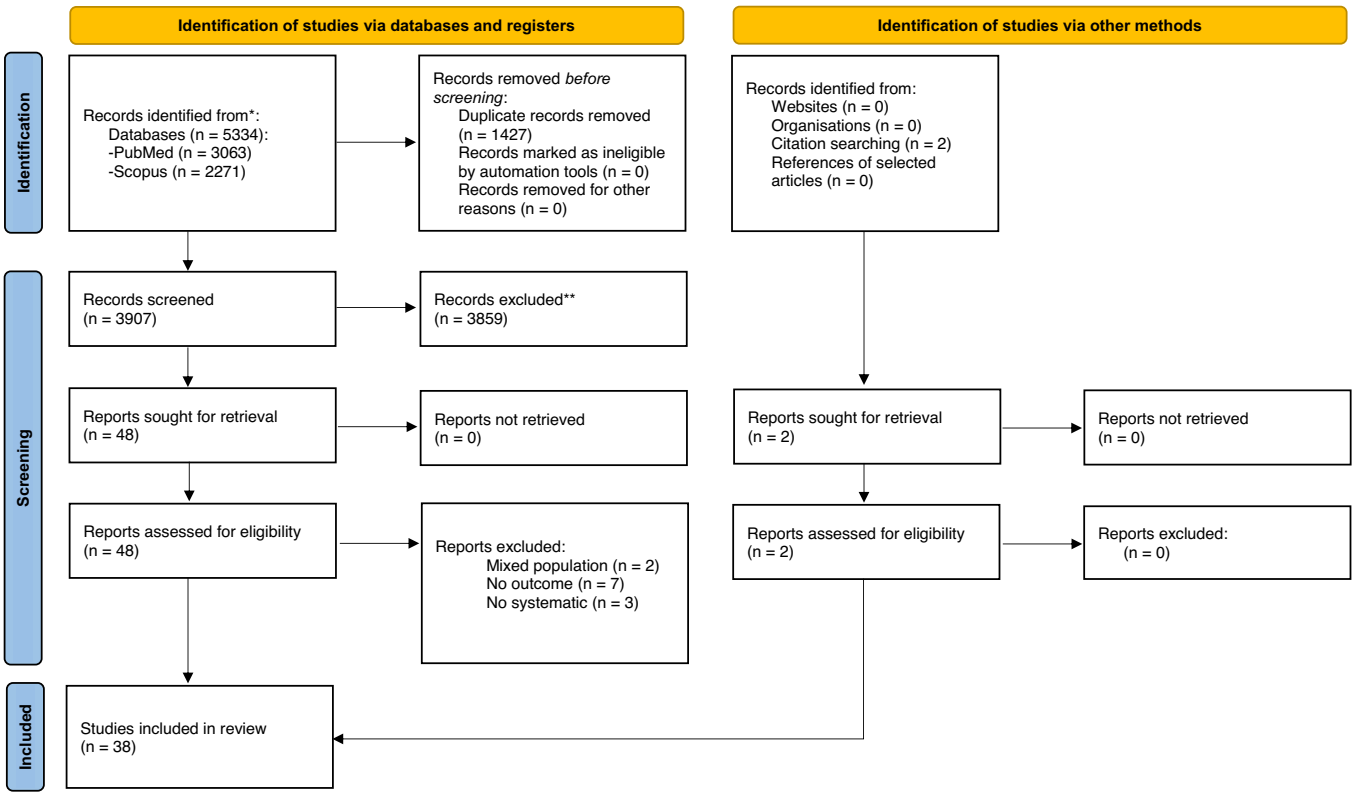
3.1. Quality assessment

Table 1 reports the quality assessment of the included studies. The overall quality score of the included studies averaged 9.16 (SD = 0.95, range 7–10).

3.2. Structural MRI

3.2.1. Whole brain

3.2.1.1. Voxel-based morphometry. Six studies adopted a whole-brain VBM approach to explore structural differences in BD subtypes (Ha et al., 2009; Caseras et al., 2013; Maller et al., 2014, 2015; Miola et al., 2022c; Thiel et al., 2024) (Table 2). Comparing patients with BD-I and HC, Miola et al., 2022c found a GM volume decrease in clusters scattered



*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).
**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

Source: Page MJ, et al. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

Fig. 1. PRISMA Flow diagram of the selection of the included studies.

bilaterally in the superior, middle, and inferior temporal gyri, in the right middle and inferior occipital gyrus, right insula, left inferior parietal lobule, and culmen, with no significant differences between BD-I and BD-II nor between BD-II and HC (Miola et al., 2022c). When considering the differences between patients with BD-I and BD-II, Caseras et al. (2013) found that patients with BD-II had significantly greater left putamen volume than patients with BD-I and that the volume of this structure correlated positively with increased left ventral striatal response during reward anticipation tasks (Caseras et al., 2013). On the other hand, Ha et al. (2009) found that patients with BD-I and BD-II exhibited GM deficits in the ventromedial prefrontal regions compared to HC, with BD-I also displaying widespread GM volume reductions bilaterally in the frontal, temporal, parietal, and parahippocampal cortices when compared with HC. However, the GM volume reductions encompassing frontal, temporal, and posterior cingulate regions found in BD-I versus BD-II did not survive multiple comparison corrections. Interestingly, age of onset negatively correlated with the GM concentrations in the bilateral medial orbitofrontal gyrus of patients with BD-II, whereas age of onset, illness duration, and depressive symptoms did not correlate with any regional volume in patients with BD-I (Ha et al., 2009). Maller and colleagues in 2014 and then in 2015 focused on differences between patient groups in GM and WM. Maller et al. (2014) reported that patients with BD-I had reduced global cortical volume as well as CT in the right medial orbitofrontal cortex, and a reduction in CT also in the left superior temporal gyrus (Maller et al., 2014). Later, Maller et al. (2015), comparing BD-I to BD-II, revealed no volumetric differences in the whole sample but only in women with an increased ratio of total brain volume (TBV) to intracranial volume (ICV) in BD-I compared to BD-II. In this sample, BD showed a decreased total GM volume but no significant differences in total brain volume, WM volume, or the ratio of TBV to ICV (Maller et al., 2015). Lastly, Thiel et al. (2024) found no differences in BD patients. However, uncorrected exploratory analyses suggested a BDI < BD-II < HC pattern in GMVs in parietal, frontal, occipital, and parahippocampal/fusiform areas (Thiel et al., 2024).

3.2.1.2. Surface-based morphometry. A general decrease in CT was found in six studies that compared BD with HC (Table 2). Thinner cortical regions were more frequent in patients with BD-I than BD-II, sometimes with a decrease in the surface area that suggested altered brain gyrification (Lyoo et al., 2006; Abé et al., 2016, 2022; Hibar et al., 2018; Woo et al., 2021; McWhinney et al., 2022). Only one study explored local gyrification in BD-I and BD-II and found no significant differences between the BD subtypes (Choi et al., 2022).

In 2006, Lyoo and colleagues described significant decreases in CT in multiple cortical areas, including the left cingulate cortex, left middle frontal cortex, left middle occipital cortex, right medial frontal cortex, right angular cortex, right fusiform cortex, and bilateral postcentral cortices in patients with BD when compared with HC. However, there were no significant differences in CT for any ROIs between subjects with BD-I ($n = 18$) and with BD-II ($n = 7$) (Lyoo et al., 2006).

Abé et al. (2016) found that patients with BD-I had significantly lower CT than those with BD-II in the right temporal lobe, with lower CT in a large cluster of medial frontal regions that did not survive correction for multiple comparisons. When comparing BD-I to HC, the first exhibited reduced CT in the left and right frontal and temporal regions, insula, pre- and postcentral regions, and medial occipital lobe with visual areas. Those with BD-II had lower CT than HC in the left and right frontal and temporal regions and the medial occipital regions, involving smaller clusters than those observed in the comparison between patients

Table 1
Demographic and study characteristics of the included studies.

First author, study year	Diagnostic criteria	Diagnosis	Population setting	Clinical scales at baseline [mean ± SD or median (minimum-maximum)]	Mood state	Illness duration (years)	BD-I N (% F) [age mean ± SD, years]	BD-II N (% F) [age mean ± SD, years]	HC Cohort, N (% F) [age mean ± SD, years]	Quality score
Altshuler et al., 1995	SADS, Research Diagnostic Criteria (at the time of DSM-IV)	BD-I BD-II	Inpatients, outpatients	NA	Euthymia	14.2 ± 8.7 18.9 ± 7.7	29 (45) [41.6 ± 11.6]	26 (50) [40 ± 10]	20 (45) [35.2 ± 9.9]	8
Hauser et al., 2000	SADS-LA, Research Diagnostic Criteria (at the time of DMV-IV)	BD-I BD-II	Inpatients, outpatients	NA	Euthymia	18.2 ± 11.8 21.1 ± 9.1	25 (52) [41.8 ± 10.5]	22 (64) [39.4 ± 10.2]	19 (48) [33.2 ± 7.1]	8.5
Brambilla et al., 2001	DSM-IV	BD BD-I BD-II	Outpatients	NA	Euthymia, depression, hypomania	16 ± 9.15	17	5	22 (36.4) [38 ± 10]	7
Brambilla et al., 2003	DSM-IV	BD BD-I BD-II	Outpatients	HRDS 11.0 ± 12.1 BRMS 1.1 ± 1.9	Euthymia, depression, hypomania	NA	18 (38.9) [34 ± 9]	6 (33.3) [38 ± 12]	36 (38.8) [37 ± 10]	7.5
Lyoo et al., 2006	DSM-IV	BD-I BD-II	Outpatients	HDRS 16.9 ± 8.8 YMRS 10.4 ± 7.8	NA	16.5 ± 11.5	18	7	21 (76.2) [31.5 ± 9.7]	7.5
Ha et al., 2009	DSM-IV	BD-I BD-II	Outpatients	HAMD 8.8 ± 6.81 (BD-I) HAMD 13.1 ± 8.31 (BD-II)	Euthymia, depression	10.4 ± 8.85 10.5 ± 7.39	23 (65.2) [35.6 ± 11.14]	23 (65.2) [35.2 ± 9.98]	23 (65.2) [36 ± 9.41]	10
Liu et al., 2010	DSM-IV-TR	BD-I BD-II	Outpatients	YMRS 0.9 ± 1.6 (BD-I) YMRS 2.0 ± 2.7 (BD-II) HAMD 6.7 ± 5.8 (BD-I) HAMD 9.5 ± 6.6 (BD-II) MADRS 5.6 ± 5.7 (BD-I) MADRS 11.5 ± 9.0 (BD-II) HARS 5.1 ± 4.7 (BD-I) HARS 10.6 ± 7.9 (BD-II)	Euthymia	7.3 ± 5.7 9.4 ± 7.4	14 (50) [35.6 ± 10.9]	13 (84.6) [35.1 ± 9.8]	21 (61.9) [38.3 ± 11.9]	10
Ha et al., 2011	DSM-IV	BD-I BD-II	Outpatients	HAMD 5.5 ± 6.90 (BD-I) HAMD 4.2 ± 4.43 (BD-II) YMRS 1.4 ± 1.51 (BD-I) YMRS 1.3 ± 1.53 (BD-II)	Euthymia, depression	13.3 ± 9.63 13.3 ± 6.28	12 (75) [37.3 ± 10.59]	12 (83.3) [35.6 ± 7.56]	22 (77.3) [34.7 ± 7.12]	10
Gutiérrez-Galve et al., 2012	DSM-IV	BD-I BD-II	Inpatients, outpatients	BDI 9.7 ± 6.7 (BD-I) BDI 12.8 ± 13.0 (BD-II)	Euthymia, depression	13.4 ± 9.0 14.9 ± 9.4	25 (60) [37.4 ± 10]	11 (72.7) [42.8 ± 7.1]	NA	9.5
Tighe et al., 2012	Research Diagnostic Criteria (RDC), DSM-III-R, DSM-IV	BD-I no psychosis BD-I with psychosis BD-II	Outpatients	NA	NA	NA	BD-I no psychosis 7 (71.4) [31.43 ± 2.39] BD-I with psychosis 26 (61.5) [34.69 ± 1.64]	12 (41.7) [33.75 ± 2.35]	31 (54.8) [32.97 ± 1.22]	7
Caseras et al., 2013	DSM-IV	BD-I BD-II	Outpatients	HDRS 3.88 ± 3.87 (BD-I) HDRS 2.67 ± 2.94 (BD-II) YMRS 3.17 ± 2.32 (BD-I)	Euthymia	NA	17 (64) [42.82 ± 7.31]	15 (60) [40.53 ± 8.09]	20 (65) [42.3 ± 5.99]	9

(continued on next page)

Table 1 (*continued*)

First author, study year	Diagnostic criteria	Diagnosis	Population setting	Clinical scales at baseline [mean ± SD or median (minimum-maximum)]	Mood state	Illness duration (years)	BD-I N (% F) [age mean ± SD, years]	BD-II N (% F) [age mean ± SD, years]	HC Cohort, N (% F) [age mean ± SD, years]	Quality score
				YMRS 1.80 ± 2.80 (BD-II)						
Maller et al., 2014	DSM IV	BD-I BD-II	Outpatients	HAMD 23.13 ± 4.24 (BD-I) HAMD 25.14 ± 4.26 (BD-II)	Depression	NA	16 (75) [39.05 ± 8.35]	15 (53.3) [47.07 ± 9.13]	31 (54.8) [39.58 ± 10.75]	10
Caseras et al., 2015	DSM IV	BD-I BD-II	Outpatients	HAMD 3.44 ± 3.52 (BD-I) HAMD 2.67 ± 2.94 (BD-II) YMRS 3.13 ± 2.39 (BD-I) YMRS 1.80 ± 2.80 (BD-II)	Euthymia	NA	16 (62) [42.56 ± 7.47]	19 (68) [38.74 ± 8.07]	20 (65) [42.3 ± 5.99]	9.5
Maller et al., 2015	DSM-IV	BD-I BD-II	Outpatients	HAMD 23.29 ± 4.15 (BD-I) HAMD 24.83 ± 4.02 (BD-II)	Depression	NA	17 (70.5) [43.12 ± 11.15]	18 (50) [48.17 ± 8.64]	36 (52.8) [42.89 ± 12.6]	10
Abé et al., 2016	DSM IV	BD-I BD-II	Outpatients	CGI-S 4.48 ± 1.42 (BD-I) CGI-S 3.83 ± 1.17 (BD-II)	Euthymia	18 ± 10 21 ± 14	81 (56) [40 ± 12]	59 (73) [40 ± 13]	85 (52) [39 ± 15]	8
Ambrosi et al., 2016	DSM IV-TR	BD-I BD-II	Outpatients	HAMD 9.2 ± 8.3 (BD-I) HAMD 14.5 ± 7.4 (BD-II) YMRS 3.2 ± 2.2 (BD-I) YMRS 3.5 ± 2.8 (BD-II)	Euthymia, depression	20.3 ± 10.7 23.9 ± 11.7	25 (48) [48.6 ± 11.4]	25 (48) [48.4 ± 12.7]	50 (48) [48.3 ± 12]	10
Cao et al., 2017	DSM-IV	BD-I BD-II MDD	Outpatients	HAMD 12.7 ± 7.9 YMRS 6.3 ± 6.8	Euthymia, depression, mania, hypomania, mixed episode	NA	NA	NA	152 (63.2) [35.4 ± 12.43]	9
Squarcina et al., 2017	DSM IV	BD-I BD-II SCZ	Outpatients	BPRS 33.0 ± 8.3 HDRS 11.5 ± 11.8 BRMRS 3.1 ± 4.4	Depression	20.8 ± 10.5 20.8 ± 10.5 20.8 ± 12.6	18	15	35 (45) [39 ± 12.6]	9
Foley et al., 2018	DSM-IV	BD-I BD-II	outpatients	HDRS 3.50 ± 3.1 (BD-I) HDRS 3.85 ± 3.7 (BD-II) YMRS 2.72 ± 2.4 (BD-I) YMRS 2.65 ± 3.0 (BD-II)	Euthymia	NA	32 (68) [45.0 ± 6.2]	34 (56) [42.8 ± 7.0]	40 (60) [43.5 ± 4.9]	9.5
Hibar et al., 2018	DSM-IV, DSM-IV-TR	BD-I BD-II	Inpatients, outpatients	NA	Euthymia, depression, mania, hypomania, mixed episode	NA	NA	NA	4056	9.5
Janiri et al., 2019	DSM-IV-TR	BD-I CT BD-I nCT BD-II CT BD-II nCT	Outpatients	HAMD 8.81 ± 5.13 (BD-I CT) HAMD 6.17 ± 5.34 (BD-I nCT) HAMD 9.88 ± 5.46 (BD-II CT) HAMD 8.82 ± 6.67 (BD-II nCT) HAMA 11.00 ± 5.77 (BD-I CT) HAMA 5.96 ± 5.06 (BD-I nCT) HAMA 11.68 ± 6.72 (BD-II CT) HAMA 8.87 ± 5.46 (BD-II nCT) YMRS 7.00 ± 5.39 (BD-I CT)	Euthymia, depression	15.44 ± 11.52 17.03 ± 12.39 16.48 ± 10.81 15.08 ± 9.76	BD-I CT 27 (62.97) [43.18 ± 11.32] BD-I nCT 29 (24.14) [44.9 ± 13.93]	BD-II CT 25 (68) [43.85 ± 12.43] BD-II nCT 23 (47.83) [44.18 ± 11.22]	HC CT 20 (50) [45.8 ± 12.12] HC nCT 61 (63.94) [44.63 ± 15.67]	10

(*continued on next page*)

Table 1 (*continued*)

First author, study year	Diagnostic criteria	Diagnosis	Population setting	Clinical scales at baseline [mean ± SD or median (minimum-maximum)]	Mood state	Illness duration (years)	BD-I N (% F) [age mean ± SD, years]	BD-II N (% F) [age mean ± SD, years]	HC Cohort, N (% F) [age mean ± SD, years]	Quality score
				YMRS 7.06 ± 8.31 (BD-I nCT) YMRS 3.76 ± 3.28 (BD-II CT) YMRS 4.26 ± 2.88 (BD-II nCT)						
Kim et al., 2020	DSM-IV-TR	BD-I BD-II	Outpatients	HDRS 6.94 ± 5.00 YMRS 1.28 ± 2.02	Euthymia, depression	4.37 ± 6.13	36 (53.33) [33.73 ± 11.32]	54	166 (57.83) [33.2 ± 12.47]	9
Kieseppä et al., 2022	DSM-IV	BD-I BD-II	Outpatients	BDI 9.0 (3–34) (BD-I) BDI 16.5 (0−30) (BD-II) HRSD 4.5 (1–19) (BD-I) HRSD 13.0 (0−21) (BD-II) YMRS 0 (0–2) (BD-I) YMRS 0 (0–1) (BD-II)	Euthymia, depression	21.9 ± 12.9 18.4 ± 4.9	8 (37.5) [46.2 ± 11.5]	8 (50) [45.5 ± 4.8]	19 (57.9) [49.6 ± 11.3]	9.5
Woo et al., 2021	DSM IV	BD-I BD-II	Outpatients	HDRS 4.77 ± 4.07 (BD-I) HDRS 8.36 ± 5.48 (BD-II) YMRS 1.97 ± 2.46 (BD-I) YMRS 0.75 ± 1.24 (BD-II) HAS 5.87 ± 4.06 (BD-I) HAS 7.80 ± 6.36 (BD-II)	Euthymia, depression	97.8 ± 95.1 50.1 ± 72.6 (months)	30 (70) [38.03 ± 11.46]	44 (66) [32.41 ± 9.80]	100 (63) [35.09 ± 11.58]	10
Yang et al., 2021	DSM IV-TR	BD MDD	Outpatients	HAMD 21.82 ± 4.48 YMRS 2.46 ± 3.17 HAMA 17.70 ± 7.04	Depression	73.5 ± 57.3 (months)	31	59	162 (58.64) [27.77 ± 5.21]	8.5
Abé et al., 2022	DSM-IV, DSM-IV-TR	BD BD-I BD-II NOS	Inpatients, outpatients	NA	Euthymia, depression, mania/mixed	NA	202 at TP1 199 at TP2	99 at TP1 97 at TP2	925 (58) [40 ± 17 at time point 1]	9.5
Choi et al., 2022	DSM-IV-TR	BD BD-I BD-II	Outpatients	HDRS 6.28 ± 4.74 YMRS 1.36 ± 2.18	Euthymia, depression	49.80 ± 66.67	30	31	183 (57) [33.49 ± 13.28]	8.5
Haukvik et al., 2022	DSM-IV or ICD-10	BD-I BD-II	Inpatients, outpatients	PANSS positive 9.1 ± 3.1 PANSS negative 9.4 ± 3.3 PANSS positive 9.0 ± 3.2 (BD-I) PANSS negative 9.2 ± 3.4 (BD-I)	NA	NA	1079 (58.1) [38.3 ± 11.9]	353	3226 (55.6) [33.3 ± 11.2]	8
Liu et al., 2022	DSM-V	BD-I BD-II	Inpatients, outpatients	HAMD 17.13 ± 7.73 (BD-I) HAMD 15.72 ± 6.48 (BD-II) YMRS 1.29 ± 1.64 (BD-I) YMRS 1.16 ± 1.82 (BD-II) HAMA 14.55 ± 8.77 (BD-I) HAMA 13.38 ± 7.34 (BD-II)	Depression	NA	31 (77.4) [25.90 ± 8.91]	32 (56.2) [23.91 ± 5.63]	79 (53.2) [27.18 ± 6.97]	10

(*continued on next page*)

Table 1 (*continued*)

First author, study year	Diagnostic criteria	Diagnosis	Population setting	Clinical scales at baseline [mean ± SD or median (minimum-maximum)]	Mood state	Illness duration (years)	BD-I N (% F) [age mean ± SD, years]	BD-II N (% F) [age mean ± SD, years]	HC Cohort, N (% F) [age mean ± SD, years]	Quality score
McWhinney et al., 2022	Scid for DSM IV	BD-I BD-II BD NOS	Inpatients, outpatients	NA	Euthymia, depression, mania, hypomania, mixed	NA	572	234	1600 (57) [35.47 ± 12.63]	8
Miola et al., 2022c	DSM V	BD-I BD-II	Outpatients	HAMD 3.9 ± 8.99 (BD-I) HAMD 1.63 ± 2.22 (BD-II) YMRS 4.57 ± 11.2 (BD-I) YMRS 1.04 ± 2.40 (BD-II) HAMA 3.9 ± 8.01 (BD-I) HAMA 1.38 ± 1.88 (BD-II) MADRS 5.0 ± 11.8 (BD-I) MADRS 2.08 ± 4.17 (BD-II) PANSS 2.95 ± 8.36 (BD-I) PANSS 0 (BD-II)	Euthymia, depression, hypomania	17.8 ± 11.4 12.8 ± 10.5	24 (25) [43.2 ± 13.7]	30 (36.67) [39.5 ± 12.4]	45 (44.45) [41.5 ± 13.1]	10
Olivito et al., 2022a	DSM-V	BD-I BD-II	Inpatients, outpatients	HDRS 1.00 ± 1.41 (BD-I) HDRS 2.62 ± 3.23 (BD-II) YMRS 1.29 ± 3.06 (BD-I) YMRS 1.77 ± 2.74 (BD-II)	Euthymia	13 ± 6.4 14 ± 14	17 (47.1) [38.6 ± 13.4]	13 (53.2) [41.2 ± 14.3]	40 (65) [41.1 ± 12.3]	10
Olivito et al., 2022b	DSM-V	BD-I BD-II	Inpatients, outpatients	HDRS 1.00 ± 1.41 (BD-I) HDRS 2.62 ± 3.23 (BD-II) YMRS 1.29 ± 3.06 (BD-I) YMRS 1.77 ± 2.74 (BD-II)	Euthymia	13 ± 6.4 14 ± 14	17 (47.05) [38.64 ± 13.48]	13 (53.84) [41.42 ± 14.38]	37 (59.46) [45.65 ± 14.15]	10
Wei et al., 2022	DSM-V	BD-I BD-II	Outpatients	HDRS 3.71 ± 5.44 (BD-I) HDRS 5.00 ± 4.93 (BD-II) YMRS 2.00 ± 3.80 (BD-I) YMRS 1.18 ± 1.78 (BD-II)	Different mood states (60.7 % of BD-I and 63.9 % of BD-II were euthymic)	NA	28 (57) [38.04 ± 13.49]	36 (61) [35.47 ± 12.05]	66 (58) [32.36 ± 9.85]	10
Canales-Rodríguez et al., 2023*	DSM-IV	BD-I BD-II	NA	NA	Euthymia	18.8 ± 9.5	107 (60) [44.4 ± 9.1]	31 (71) [46.8 ± 7.7]	158 (60.13) [44.1 ± 9.1]	9
Matsumoto et al., 2023	DSM-IV, DSM-IV-TR, DSM-V	BD-I BD-II	Inpatients, outpatients	NA	NA	13.0 ± 10.8	BD 237	NA	3068	10
Mørch-Johnsen et al., 2023	DSM-IV	BD-I BD-II	Outpatients	YMRS 2 ± 4 IDS-C 15 ± 16 PANSS 43 ± 11	36.4 % euthymic	10.3 ± 10.8	183	125	826 (45.9) [33.8 ± 14.2]	9.5
Thiel et al., 2024	DSM-IV-TR	BD-I BD-II	Outpatients	HDRS 6.82 ± 6.52 (BD-I) HDRS 8.30 ± 6.48 (BD-II) YMRS 3.61 ± 5.58 (BD-I) YMRS 3.87 ± 5.51 (BD-II)	Euthymia, depression, (hypo) mania or mixed episode	17.75 ± 11.19 16.3 ± 8.8	73 (57.5) [41.77 ± 11.51]	63 (52.4) [40.48 ± 12.56]	136 (56.6) [42.46 ± 12.92]	10

Legend. BD-I, bipolar disorder type I; BD-II, bipolar disorder type II; HC, healthy controls; SD, standard deviation; NA, not available; DSM, Diagnostic and Statistical Manual of Mental Disorders; SADS, Schedule for Affective Disorders and Schizophrenia; SADS-LA, Schedule for Affective Disorders and Schizophrenia-Lifetime Version; MDD, major depressive disorder; SCZ, schizophrenia; BDI, Beck's Depression Inventory; BRMS, Bech–Rafaelsen Mania Scale; BPRS, Brief Psychiatric Rating Scale; CGI-S, Clinical Global Impression; CT, childhood trauma; HRDS, Hamilton Depression Rating Scales; HAMD, 17-item Hamilton Depression Rating Scale; HARS, Hamilton Anxiety Rating Scale; HAS, Hamilton Anxiety Rating Scale; IDS-C, Inventory of Depressive Symptoms - Clinician Rated; PANSS, Positive and Negative Syndrome Scale; YMRS, Young Mania Rating Scale; TP1, time point 1 (baseline); TP2, time point 2 (follow-up).

* From a total of BD-I ($n = 101$) and BD-II ($n = 37$), patient characteristics are provided for the subset of patients ($n = 138$) without missing data.

with BD-I and HC (Abé et al., 2016).

Interestingly, a multicenter longitudinal MRI study conducted by the ENIGMA BD Working Group identified thickness differences in limbic areas between the BD-I and BD-II groups, particularly in the right parahippocampal gyri, with patients with BD-I showing a decline in right parahippocampal thickness. In contrast, those with BD-II displayed thickness increases in the same region (Abé et al., 2022). Of note, a decreased surface area affecting the right insula was described by Woo et al. (2021) in patients with BD-II compared to those with BD-I. Moreover, patients with BD-I showed thinner cortical regions than those with BD-II and HC in the pars triangularis, left pars opercularis, and right pars orbitalis of the inferior frontal gyrus and the right orbital gyrus. However, the left pars orbitalis showed significant cortical thinning in BD-II but not in BD-I (Woo et al., 2021). McWhinney et al. (2022) demonstrated that people in the low-thickness cluster with a thinner cortex, especially in the frontal and temporal lobes, were more likely to have the diagnosis of BD-I than BD-II. Conversely, differences in surface area did not differ between BD subtypes (McWhinney et al., 2022). Lastly, Hibar et al. (2018) and Matsumoto et al. (2023) found no significant differences in CT or surface area between patients with BD-I or BD-II. Notably, the authors evidenced an association between the duration of illness and CT, which may also interact with medication status (Hibar et al., 2018).

3.2.2. Region of interest (ROI)-based

Frontal and temporal lobes. Regarding the differences in frontal and temporal structures between BD-I and BD-II, one MRI investigation explored GM volume differences in 22 frontal and temporal ROIs (Yang et al., 2021), two studies investigated volumetric differences in regions belonging to the frontal lobes (Gutiérrez-Galve et al., 2012; Yang et al., 2021), one study limited its analysis to the temporal lobes (Brambilla et al., 2003), and another investigated the temporal lobes and hippocampus (Hauser et al., 2000). Yang et al. (2021) found no significant volumetric difference between BD-I and BD-II. However, when patient groups were compared to HC, BD-I showed lower GM volumes in the left inferior temporal gyrus, left temporal pole, and bilateral rostral middle frontal gyrus. In contrast, BD-II exhibited lower GM volumes in the left temporal pole (Yang et al., 2021). Gutiérrez-Galve et al. (2012) studied the cortical thickness (CT), surface area, and volume of six frontal and six temporal ROIs. They found no significant difference between BD-I and BD-II in total brain volume, in frontal or temporal CT or surface area, or in the strength of the association between premorbid IQ, memory, and executive functions, and frontal cortical measures (Gutiérrez-Galve et al., 2012). Brambilla et al. (2003), investigating a variety of temporal structures, showed that the left amygdala was significantly larger in patients with BD than in HC, with no significant differences between small samples of BD-I ($n = 18$) and BD-II ($n = 6$). The hippocampus, superior temporal gyri, and temporal lobe volume also showed no significant differences between BD and HC, nor between BD-I and BD-II (Brambilla et al., 2003). Conversely, Hauser and colleagues found that BD-I had significantly larger lateral ventricle area and the lateral ventricle to cerebrum area ratio in the left hemisphere than those with BD-II or HC, with such measures being approximately twice as large in the BD-I group as in the other groups (Hauser et al., 2000).

Hippocampus. Some studies (Cao et al., 2017; Janiri et al., 2019; Haukvik et al., 2022) specifically investigated hippocampal volume differences between BD subtypes. Janiri et al. (2019) performed a VBM study on hippocampal subfields (CA1, CA2/3, CA4/dentate gyrus, presubiculum, and subiculum) for both hemispheres, showing no significant differences between BD-I and BD-II. However, compared to HC, both BD-I and BD-II presented lower volumes in all hippocampal subfields (Janiri et al., 2019). Similarly, Haukvik et al. (2022) found no significant differences in the whole hippocampus volume or its subfields between BD-I and BD-II. Also, when compared to HC, BD-II showed no difference in whole hippocampus volume. In contrast, BD-I presented lower whole hippocampal volumes, which sustained across most subfields, including the hippocampal tail, subiculum, presubiculum, CA1, CA2/3, CA4, molecular layer, granule cell layer of the dentate gyrus, and the hippocampal amygdala transition area (Haukvik et al., 2022). Consistent with the previous findings, Cao et al. (2017) identified lower hippocampal volumes in BD compared to HC, and further post hoc *t*-tests within BD subtypes revealed that this difference was driven mainly by BD-I, with no significant difference in hippocampal subfield volumes in BD-II compared to HC (Cao et al., 2017).

Basal ganglia and thalamic nuclei. Brambilla et al. (2001) performed an MRI study of the basal ganglia in patients with BD. They found that caudate, putamen, and total globus pallidus volumes, after correction for ICV, were not significantly different between BD and HC (Brambilla et al., 2001). In addition, Mørch-Johnsen et al. (2023), investigating thalamic nuclei volumes, found that BD had significantly smaller volumes in the mediodorsal medial magnocellular, lateral geniculate, medial geniculate, and pulvinar anterior compared to HC (Mørch-Johnsen et al., 2023). Interestingly, BD-I showed significantly smaller volumes of mediodorsal lateral parvocellular, mediodorsal medial magnocellular, and pulvinar anterior compared with BD-II (Mørch-Johnsen et al., 2023).

Cerebellum. Two studies (Kim et al., 2020; Olivito et al., 2022a) investigated morphological features of the cerebellum in BD. Olivito et al. (2022a) found a significant cerebellar GM reduction in both BD-I and BD-II when compared to HC, with a more diffuse involvement in BD-II than BD-I, and with both patient groups showing a pattern of cerebellar GM reduction in the right lobule I-IV, V, Crus I, and Crus II, and the left Crus II and vermis Crus II (Olivito et al., 2022a). Similarly, Kim et al. (2020) found a reduced cerebellar volume in BD compared to HC, which was limited to the left lobule IX. Furthermore, the same authors found a significant increase in the CT of all cerebellar subregions in the BD group compared to HC, with the comparison between BD-I and BD-II showing no significant differences in cerebellar CT or subregional volumes (Kim et al., 2020).

3.3. White matter

3.3.1. Diffusion indexes and tractography

Studies examining WM abnormalities in individuals with BD yielded mixed results (Table 2). Ambrosi et al. (2016) observed increased FA in the right inferior longitudinal fasciculus in BD-I compared to BD-II, while Ha et al. (2011) reported the opposite direction (Ha et al., 2011; Ambrosi et al., 2016). Liu et al. (2010) found increased FA values in BD-I in the right precuneus, right inferior frontal gyrus, and left inferior prefrontal area compared to BD-II (Liu et al., 2010). Maller et al. (2014) observed increased MD in several brain regions, including the brain stem, internal capsule, middle temporal gyrus, putamen, and thalamic radiation, showing higher values in BD-I than BD-II. Additionally, RD was increased in patients with BD-I compared to BD-II in the insular area (Maller et al., 2014). The same study of occipital lobe asymmetry in patients with BD found an increased prevalence of occipital bending in BD-I and BD-II than in HC (Maller et al., 2015).

Ha et al. (2011) also studied mean apparent diffusion coefficient (ADC) maps, revealing lower ADC values in specific regions in BD-I compared to BD-II in the left frontal, right parietal, temporal regions, and right thalamus (Ha et al., 2011).

Two other studies (Squarcina et al., 2017; Kieseppä et al., 2022) included a comparison group with a different psychiatric diagnosis and patients with BD. Squarcina et al. (2017) found that both BD and SCZ showed decreased FA and increased MD, volume ratio (VR), AD, and RD when compared to HC, with overlapping affected areas in both BD and

Table 2
Summary of neuroimaging findings from the included studies comparing BD-I and BD-II.

First author, study year	Study design	Country	Field strength (Tesla)	Imaging software	Space/Atlas	Type of MRI [main outcome (s)]	Whole brain/ROI	Main findings
Altshuler et al., 1995	Cross-sectional	USA	0.5	Neuroradiologist (double blind reading)	NA	sMRI [hyperintensities of GM and WM]	Whole brain	**BD-I vs BD-II**: 62 % of the BD-I had signal hyperintensities in the periventricular regions, compared to 38 % of the BD-II. **BD-I vs HC**: 30 % of the HC had signal hyperintensities in the periventricular regions. The tendency for BD patients to have periventricular hyperintensities appeared only after age 30.
Hauser et al., 2000	Cross-sectional	USA	0.5	DAGE 65; - Camera to computer than rendering HR with PVM - Manual volume extraction by blind to diagnosis	NA-MRI atlas	sMRI [volume, area, ratio]	ROI (temporal lobes and hyppocampus)	**BD-I vs BD-II**, **BD-I vs HC**: ↑ left temporal lobe volume, ↑ left lateral ventricular size, ↑ LV/C area ratio in the left hemisphere. In the right temporal lobe, the measures of left and right inferior horns of the lateral ventricles and the third ventricle were not significantly different among diagnostic groups.
Brambilla et al., 2001	Cross-sectional	USA	1.5	Scion Image Beta-3b	Traced manually by standard brain atlas	sMRI [volume]	ROI (basal ganglia)	**BD vs HC**: no significant differences for any of the basal ganglia measures. **BD-I vs BD-II**: illness duration inversely correlated with basal ganglia volumes more for BD-I than BD-II.
Brambilla et al., 2003	Cross-sectional	USA	1.5	Scion Image Beta-3b	Traced manually by standard brain atlas	sMRI [volume]	ROI (temporal structures)	**BD vs HC**: the left amygdala was significantly larger in BD than HC. **BD-I vs BD-II**: no significant differences were found for any anatomical measures between BD-I and BD-II.
Lyoo et al., 2006	Cross-sectional	USA	1.5	FreeSurfer	Desikan-Killiany atlas	sMRI [CT]	Whole brain and ROI	**BD vs HC**: ↓ CT in the frontal, cingulate and middle-occipital cortices. **BD-I vs BD-II**: no significant differences in CT for any ROI. **BD-I vs HC**: similar to BD vs HC. **BD-II vs HC**: similar to BD vs HC.
Ha et al., 2009	Cross-sectional	Korea	1.5	SPM2	Talairach	sMRI [VBM]	Whole brain	**BD-I vs BD-II**: ↓ GM volume in the frontal, temporal, and posterior cingulate regions in BD I compared with BD-II did not survive FDR correction. **BD-II vs HC**: ↓ GM in

(*continued on next page*)

Table 2 (*continued*)

First author, study year	Study design	Country	Field strength (Tesla)	Imaging software	Space/Atlas	Type of MRI [main outcome (s)]	Whole brain/ROI	Main findings
								the bilateral ventromedial prefrontal regions and right superior frontal gyrus. **BD-I vs HC**: ↓ GM in same regions as BD II and in the bilateral frontal, temporal, parietal, and parahippocampal regions.
Liu et al., 2010	Cross-sectional	Taiwan	1.5	FMRIB, BIRT	MNI	DTI [FA]	Whole brain	**BD-I vs BD-II**: ↑ FA in the right precuneus, right inferior frontal gyrus, and left inferior prefrontal area. **BD-I and BD-II vs HC**: ↓FA in the right thalamus and right subgenual anterior cingulate cortex. **BD-I vs HC**: ↓FA in the right thalamus, right subgenual anterior cingulate cortex, right inferior frontal area, and left rostral anterior cingulate cortex. **BD-II vs HC**: ↓FA in the bilateral subgenual anterior cingulate, right inferior frontal, left middle temporal, and left inferior temporal areas.
Ha et al., 2011	Cross-sectional	Korea	1.5	FMRIB, SPM8	MNI	DTI [FA, ADC]	Whole brain	**BD-I vs BD-II**: ↓ FA in the inferior longitudinal fasciculus. ↓ADC in the left frontal, right parietal, temporal regions and in the right thalamus. **BD-I vs HC**: ↓ FA in the corpus callosum, left cingulum, superior longitudinal fasciculus, inferior fronto-occipital fasciculus and uncinate fasciculus, inferior longitudinal fasciculus and in the left parietal associations fibers region. ↑ ADC in the bilateral frontal, anterior cingulate, insular and in the temporal regions. **BD-II vs HC**: ↓ FA in the right anterior and posterior cingulum, body and splenium of corpus callosum, and in the right medial prefrontal white matter. ↑ ADC in the bilateral frontal, anterior

(*continued on next page*)

Table 2 (*continued*)

First author, study year	Study design	Country	Field strength (Tesla)	Imaging software	Space/Atlas	Type of MRI [main outcome (s)]	Whole brain/ROI	Main findings
								cingulate, insular and in the temporal regions in both BD-I and BD-II compared with HC.
Gutiérrez-Galve et al., 2012	Cross-sectional	UK	1.5	FreeSurfer 4.3.0	Desikan template	sMRI [volume, CT, SA]	ROI (6 frontal and 6 temporal parcellations)	**BD-I vs BD-II**: no significant differences in total brain volume, frontal or temporal CT.
Tighe et al., 2012	Cross-sectional	USA	1.5	Locally developed imaging software	NA	sMRI [WMH volume]	Whole brain	**BD-I vs BD-II**, **BD-I vs HC**, **BD-II vs HC**: Absence of an overall significant difference in total WMH volume by group. The mean total volume of WMH in BD-I with psychotic features was significantly higher compared with HC.
Caseras et al., 2013	Cross-sectional	USA	3	FMRIB, FreeSurfer	MNI	fMRI [task fMRI]	Whole brain and ROI (ventral striatum)	**BD-I vs BD-II**: ↓bilateral ventral striatal activity for reward anticipation; ↑right ventral striatal activity for positive outcome. - whole brain analysis: ↓ in the left ventrolateral prefrontal cortex, insula, precentral gyrus, and middle and superior temporal cortex during reward anticipation; no difference in activation to positive outcome. - striatal GM volume: ↓left putamen volume. **BD-I vs HC**: no significant difference for reward anticipation or positive outcome; - Whole brain analysis: no difference in activation for reward anticipation or positive outcome. **BD-II vs HC**: ↑ bilateral ventral striatal activity for reward anticipation; - Whole brain analysis: ↑ in the left ventrolateral prefrontal cortex, insula, precentral gyrus, middle and superior temporal cortex, caudate nuclei bilaterally, and the left dorsolateral prefrontal cortex during reward anticipation; no difference in activation to positive outcome;

(*continued on next page*)

Table 2 (*continued*)

First author, study year	Study design	Country	Field strength (Tesla)	Imaging software	Space/Atlas	Type of MRI [main outcome (s)]	Whole brain/ROI	Main findings
Maller et al., 2014	Cross-sectional	Australia	1.5	FreeSurfer, Qdec, FMRIB, TBSS	MRI Atlas of Human White Matter	sMRI [CT, volume] DTI [FA, L1, MD, RD]	Whole brain	- Striatal GM volume: ↑ left putamen volume **BD-I vs BD-II**: ↓cortical volume in the right medial orbitofrontal region; ↓ CT in the right medial orbitofrontal region and left superior temporal gyrus. No significant subcortical volumetric differences. MD: ↓ strong trends in the brain stem, internal capsule, middle temporal gyrus, putamen, anterior thalamic radiation, ILF/FOF, SLF, superior corona radiata, and right anterior thalamic radiation; RD: ↓ strong trend in the left posterior limb of the internal capsule, pallidum, SLF, superior corona radiata, and ILF/FOF in the region of the insula. **BD vs HC**: significant differences in terms of GM, WM; TBV/ICV was ↓ in BD. **BD-I vs HC**: similar to BD vs HC. No significant differences in FA. **BD-II vs HC**: similar to BD vs HC, although TBV/ICV did not differ. FA differences in widespread regions including the corpus callosum, internal capsules, SLFs, ILF/FOFs; RD differences included the cingulate, the anterior thalamic radiations and brain stem.
Caseras et al., 2015	Cross-sectional	UK	3	FMRIB, ExploreDTI	MNI	fMRI [task fMRI] DTI [FA]	Whole brain and ROI (DLPFC, amygdala, and accumbens)	**BD-I vs BD-II**: ↑ BOLD within the working memory network for 2-back + no-distracters >0-back + no-distracters. With fear distracter: ↓ activity in the DLPFC and amygdala. DTI: ↓ FA in the right uncinate fasciculus; ↑ RD. **BD-I vs HC**: ↑ BOLD within the working memory network for 2-back + no-distracters >0-back + no-distracters. DTI: ↓ FA in the right uncinate fasciculus; ↑ RD.

(*continued on next page*)

Table 2 (*continued*)

First author, study year	Study design	Country	Field strength (Tesla)	Imaging software	Space/Atlas	Type of MRI [main outcome (s)]	Whole brain/ROI	Main findings
								BD vs HC: DTI: no significant group differences in FA in the comparison tract or in the left uncinate fasciculus; ROI analyses comparing BOLD responses for each distracter showed modulation of the amygdala activity dependent on patient group and type of distracter. Functional connectivity analysis (PPI): BD-II vs BD-I and vs HC ↑ negative correlation between the DLPFC and amygdala, bilaterally, during the presence of fear distracters.
Maller et al., 2015	Cross-sectional	Australia	1.5	FreeSurfer	MNI305 template	sMRI [OB, volume]	Whole brain	**BD-I vs BD-II**: ↑ratio of TBV to ICV among females with BD-I when compared with females with BD-II. **BD vs HC**: ↓ mean total GM volume; ↓ right and left hippocampal volumes, in particular the right hippocampal volumes for males.
Abé et al., 2016	Cross-sectional	Sweden	1.5	FreeSurfer 5.1	Desikan–Killiany atlas	sMRI [VBM, CT, SA]	Whole brain	**BD-I vs BD-II**: ↓CT in the right temporal lobe. **BD-I vs HC**: ↓CT in the left and right frontal and temporal regions, insula, pre- and postcentral regions and medial occipital lobe (including visual areas). **BD-II vs HC**: ↓CT in the left and right frontal and temporal regions and in medial occipital regions.
Ambrosi et al., 2016	Cross-sectional	Italy	3	FSL 4.1	MNI	DTI [FA, AD, RD]	Whole brain	**BD-I vs BD-II**: FA: ↑ in the right inferior longitudinal fasciculus (ILF); AD: no significant differences; RD: no significant differences; **BD-I vs HC**: AD: ↓ in wide clusters bilaterally distributed over the cerebellum, right corticospinal tract (from the brainstem to the parietal lobe), left ILF and left internal capsule; RD: ↓ in the left internal capsule, the left ILF, in the fronto-parietal lobe and

(*continued on next page*)

Table 2 (*continued*)

First author, study year	Study design	Country	Field strength (Tesla)	Imaging software	Space/Atlas	Type of MRI [main outcome (s)]	Whole brain/ROI	Main findings
								bilaterally in the cerebellum. **BD-II vs HC**: FA: ↓ in the left fornix and left parietal lobe AD: similar to BD-I; RD: ↓ in the left internal capsule.
Cao et al., 2017	Cross-sectional	USA	1.5	FreeSurfer 5.3	NA	sMRI [volume]	ROI (hyppocampus)	**BD-I vs BD-II**: ↓ volume relatively more severe in BD-I than BD-II, which spread across all the subfields of the hippocampus. Significant negative correlations between the number of manic episodes and both sides of CA3, CA4 and hippocampal tail, while no significant correlation between the number of hypomanic, mixed and depressive and hippocampal subfield volumes in BD-I. A positive correlation between the left hippocampal tail volume and the number of hypomanic episodes in BD-II. **BD vs HC**: ↓ hippocampal subfield volumes in BD majorly driven by BD-I, although BD-II showed non-significant decrease of the hippocampal subfield volumes.
Squarcina et al., 2017	Cross-sectional	Italy	1.5	FSL	JHU ICBM-DTI-81 tract atlas	DTI [MD, VR, RD, AD, FA, MO]	Whole brain	**BD-I vs BD-II**: no differences in diffusion indexes. **BD vs HC**: FA, MD, VR, AD and RD showed significant changes, in particular in the corpus callosum, external and internal capsule, corona radiata, and longitudinal fasciculus. **BD vs SCZ**: no differences in diffusion indexes.
Foley et al., 2018	Cross-sectional	UK	3	ExploreDTI version 4.8.3	MNI	DTI [FA]	ROI (Uncinate fasciculus, cingulum body, and parahippocampal cingulum)	**BD-I vs BD-II**: ↓FA in left and right uncinate fasciculus. **BD-I vs HC**: ↓FA in left and right uncinate fasciculus. **BD-II vs HC**: no significant differences. **BD-I siblings vs HC**: ↓FA in left uncinate fasciculus. **BD-I/BD-II vs siblings**: no

(*continued on next page*)

Table 2 (*continued*)

First author, study year	Study design	Country	Field strength (Tesla)	Imaging software	Space/Atlas	Type of MRI [main outcome (s)]	Whole brain/ROI	Main findings
								significant differences.
Hibar et al., 2018	Cross-sectional	Multicentric	1,5/3	FreeSurfer	Desikan–Killiany atlas	sMRI [CT, SA]	Whole, parameter for 70 cortical ROIs: 68 regions and two whole hemisphere	**BD-I vs BD-II**: no significant differences in CT or surface area ROIs. **BD vs HC**: significant and widespread pattern of reduced CT, with the largest effects in the left pars opercularis, left fusiform gyrus and left rostral middle frontal cortex.
Janiri et al., 2019	Cross-sectional (and longitudinal for supplemental analysis)	Italy	3	FreeSurfer 5.3	Talairach	sMRI [VBM]	ROI (hippocampal subfields)	**BD-I vs BD-II**: no significant differences in hippocampal subfield volumes. **BD-I vs HC**: ↓ all hippocampal subfield volumes. **BD-II vs HC**: ↓ all hippocampal subfield volumes.
Kim et al., 2020	Cross-sectional	Korea	3	CERES, ANTs	MNI152 template	sMRI, [CT, volume]	ROI (Cerebellum)	**BD-I vs BD-II**: no significant difference in the cerebellar subregional CT and volumes. **BD vs HC**: ↑ CT in all cerebellar subregions except for the left lobule IV; no significant difference in the total cerebellar volume and in all cerebellar subregional volumes except for the left lobules VIIIA, IX, and right lobule IX.
Kieseppä et al., 2022	Longitudinal	Finland	1,5 at t1, 5 at t1	FMRIB	MNI 152	DTI [WMH, FA]	Whole brain	**BD-I vs BD-II**: occurrence of periventricular WMHs (PVHs) at follow-up. [In the BD-I group, on follow-up MRI the most typical localization of the DWMHs was the right frontal lobe, 20/53), in the BD-II group both the right frontal (13/57) and left frontal (14/57) lobes.] Only BPII patients showed WMHs in basal nuclei. **BD-I vs HC**: occurrence of periventricular WMHs (PVHs) at follow-up. ↓FA [reaching anteriorly the left superior frontal gyrus WM (forceps minor) and posteriorly the left superior parietal lobule WM (forceps major)], ↑MD [in the same areas and also in the left posterior corona radiata, left

(*continued on next page*)

Table 2 (*continued*)

First author, study year	Study design	Country	Field strength (Tesla)	Imaging software	Space/Atlas	Type of MRI [main outcome (s)]	Whole brain/ROI	Main findings
								cingulum, and left precuneus] and ↑RD values [in the same areas as increased MD and also in the left occipital gyri] in the corpus callosum. **BD-II vs HC**: no significant difference in FA, MD, or RD values.
Woo et al., 2021	Cross-sectional	Korea	3	FreeSurfer 5.3	Talairach	sMRI [SA, CT]	Whole brain	**BD-I vs BD-II**: ↑ SA in the right long insula; No significant differences in CT. **BD vs HC**: widespread cortical thinning in the bilateral frontal, temporal, and occipital regions; cingulate gyrus; and insula. Some areas of the VLPFC and the OFC showed significant cortical thinning only in BD-I compared with HCs; the left pars orbitalis showed significant cortical thinning in BD-II but not in BD-I compared with HCs. ↓ SA with the largest differences in the left long insula, right straight gyrus, left pars orbitalis, right anterior cingulate gyrus, right posterior mid-cingulate gyrus, right lateral superior temporal gyrus, right subcentral gyrus, right cuneus, right superior frontal gyrus, and right lingual gyrus. ↑ SA in the right pars triangularis, right ventral posterior cingulate, right middle frontal gyrus, and right anterior temporal gyrus.
Yang et al., 2021	Cross-sectional	China	3	FreeSurfer 6.0	Desikan-Killiany atlas	sMRI [volume]	ROI (22 regions from temporal and frontal lobes)	**BD-I vs BD-II**: no significant differences. **BD-I vs HC**: ↓ GM volume in the left inferior temporal gyrus, left temporal pole and bilateral RMFG. **BD-II vs HC**: ↓ GM volume in the left temporal pole. **BD vs HC**: ↓ GM volume in the bilateral RMFG, left temporal pole and rSTG.

(*continued on next page*)

Table 2 (*continued*)

First author, study year	Study design	Country	Field strength (Tesla)	Imaging software	Space/Atlas	Type of MRI [main outcome (s)]	Whole brain/ROI	Main findings
Abé et al., 2022	Longitudinal	Multicentric ENIGMA 14 sites	1.5, 3	FreeSurfer	Desikan-Killiany atlas	sMRI [volume, CT, SA]	Whole brain	**BD-I vs BD-II**: BD-I showed a decline in right parahippocampal CT, whereas BD-II showed CT increase in the same region. **BD vs HC**: ↑cortical thickness change rates in the bilateral fusiform, left medial orbitofrontal, bilateral parahippocampal, right inferior temporal, and right isthmus cingulate cortex; ↓change rates in caudate and ↑ change rates in ventricle volumes. Faster increases over time in thickness change rates in ventricular volume, right fusiform, and right parahippocampal remained significant after correcting for multiple comparisons. No significant differences in SA change rates.
Choi et al., 2022	Cross-sectional	Korea	3	FreeSurfer 5.3	Desikan–Killiany atlas	sMRI [LGI]	Whole brain	**BD-I vs BD-II**: no significant differences. **BD-I vs HC**: ↓ LGI in the precentral gyrus and transverse temporal cortex. **BD-II vs HC**: ↓ LGI in the transverse temporal cortex and insular cortex.
Haukvik et al., 2022	Cross sectional	Multicentric	1.5, 3	FreeSurfer 6.0.0	Desikan–Killiany atlas	sMRI [VBM]	ROI (hippocampus and subregions)	**BD-I vs BD-II**: no significant volumetric differences. **BD-I vs HC**: ↓ whole hippocampus volume, present across most subfields. **BD-II vs HC**: no significant difference in whole hippocampus volume.
Liu et al., 2022	Cross-sectional	China	3	SPSS v 26.0	MNI	fMRI [functional-dynamic ALFF]	Whole brain	**BD-I vs BD-II**: ↓ dALFF values in the rSTG and MTG. **BD I and BD II vs HC**: ↓ dALFF values in the superior, middle and inferior frontal gyrus, superior, middle and inferior temporal gyrus, cuneus, precuneus, cingulum, insula, occipital lobe regions, inferior parietal gyrus, pre-central and postcentral gyri, and the medial part of the temporal lobe

(*continued on next page*)

Table 2 (*continued*)

First author, study year	Study design	Country	Field strength (Tesla)	Imaging software	Space/Atlas	Type of MRI [main outcome (s)]	Whole brain/ROI	Main findings
								(including the hippocampus). **BD-I vs HC**: ↓ dALFF values in the right supramarginal gyrus and postcentral gyrus.
McWhinney et al., 2022	Cross-sectional	Multicentric ENIGMA 14 sites	1.5, 3	FreeSurfer	Desikan-Killiany atlas	sMRI [CT, SA]	Whole brain	**BD-I vs BD-II**: people in the low-thickness cluster had thinner cortex, especially in the frontal and temporal lobes, and were more likely to have the diagnosis of BD-I than BD-II. SA cluster were no related to BD subtypes. **BD vs HC**: people in the low-thickness cluster were more likely to have the diagnosis of BD. SA cluster were no related to BD diagnosis.
Miola et al., 2022c	Cross-sectional	Italy	3	SPM (CAT12)	MNI	sMRI [VBM, SBM]	Whole brain	**BD-I vs BD-II**: no significant differences. **BD-I vs HC**: ↓ GMV in seven clusters located bilaterally in the superior, middle, and inferior temporal gyri, in the right middle and inferior occipital gyrus, right insula, left inferior parietal lobule, and culmen. **BD-II vs HC**: no significant differences.
Olivito et al., 2022a	Cross-sectional	Italy	3	FMRIB, SPM, SUIT	Probabilistic cerebellar atlas (SUIT)	sMRI [VBM]	ROI (cerebellum)	**BD-I and BD-II vs HC**: a pattern of overlapping ↓ cerebellar GM involving the right lobule I-IV, V, Crus I and Crus II and the left Crus II and vermis Crus II. **BD-I vs HC**: ↓ GM density both at the level of the anterior and posterior cerebellar portions with main involvement of the right hemisphere with a single large cluster of ↓ GM with peak voxels in the right lobule V. **BD-II vs HC**: diffuse ↓ cerebellar GM at both the left and right hemispheres, involving the right lobule I-IV, V, VI, crus I, crus II, IX and VIIIb, the left VI, crus I, crus II, VIIb and IX, and the vermis crus II.

(*continued on next page*)

Table 2 (*continued*)

First author, study year	Study design	Country	Field strength (Tesla)	Imaging software	Space/Atlas	Type of MRI [main outcome (s)]	Whole brain/ROI	Main findings
Olivito et al., 2022b	Cross-sectional	Italy	3	SPM8	MNI	fMRI [FC]	ROI (cerebellar dentate nucleus)	**BD-I vs BD-II**: no significant differences in cerebellar-cerebral FC. **BD-II vs HC**: ↑FC between the left dentate nucleus and the right parahippocampal gyrus and right lateral occipital cortex. Similarly, ↑FC between the right dentate nucleus and the left posterior cingulate gyrus, the right pulvinar, and the right angular gyrus. **BD-I vs HC**: ↑FC between the left dentate nucleus and the left temporal fusiform cortex, right hippocampus, and left posterior cingulate gyrus and ↓ FC with the right temporal pole. ↑FC between the right dentate nucleus and the left posterior cingulate gyrus and ↓ FC with right temporal fusiform cortex.
Wei et al., 2022	Cross-sectional	Taiwan	3	SPM12	MNI	fMRI [FC]	ROI (caudate)	**BD-I vs BD-II**: ↓FC between the DC and the OFC. **BD-II vs HC**: ↓FC between the DC and the OFC, vlPFC, dorsolateral prefrontal cortex, posterior parietal cortex, inferior temporal gyrus, parahippocampal gyrus, supplementary motor area, thalamus, pons, and cerebellum. **BD-I vs HC**: ↓FC between the DC and the putamen and parahippocampal gyrus.
Canales-Rodríguez et al., 2023	Cross-sectional	Spain	3	FSL	'JHU ICBM-DTI-81 White-Matter Labels'; 'JHU White-Matter Tractography Atlas'; 'MNI Structural Atlas'; 'Harvard-Oxford Cortical Structural Atlas'; 'Harvard-Oxford Subcortical Structural Atlas'; 'Cerebellar Atlas in MNI152 space after normalisation with FNIRT', as well as the Anatomical Automatic Labelling atlas	DTI [MD, FA] SMT [IASF, Dpar]	Whole brain	**BD-I vs BD-II**: no significant differences in MD, FA, IASF, Dpar. **BD vs HC**: FA: ↓ in the body of the corpus callosum, cerebral peduncle, WM regions adjacent to temporal and parietal lobes, corticospinal tract, and inferior longitudinal fasciculus. MD: ↑ in the genu and body of the corpus callosum, superior and posterior corona radiata, the insula,

(*continued on next page*)

Table 2 (*continued*)

First author, study year	Study design	Country	Field strength (Tesla)	Imaging software	Space/Atlas	Type of MRI [main outcome (s)]	Whole brain/ROI	Main findings
								Heschl's gyrus, cerebellum, superior frontal orbital cortex, supramarginal gyrus, and middle temporal. IASF: ↓WM in the body and splenium of the corpus callosum, cingulum bundle, and medial lemniscus. IASF: ↓GM in the cerebellum, inferior temporal gyrus, lateral occipital cortex, frontal pars triangularis, and medial frontal gyrus. Dpar: ↑ in the frontal lobe, cingulum, olfactory, calcarine, insula, Heschl's gyrus, rolandic operculum, temporal and occipital lobes, fusiform, and lingual gyrus
Matsumoto et al., 2023	Cross-sectional	Japan	1.5 T 3 T	FreeSurfer 5.3	Desikan-Killiany atlas	sMRI [CT, surface area, volume]	68 ROIs for CT and surface area	**BD-I vs BD-II**: no significant difference for bilateral hemisphere CT and SA. CT: SCZ < BD < MDD Cortical SA: SCZ < BD, MDD < BD
Mørch-Johnsen et al., 2023	Cross-sectional	Norway	3	FreeSurfer 6.0.0	Histology-based postmortem atlas combined with image tissue contrast	sMRI	Thalamic nuclei volumes	**BD-I vs BD-II**: ↓ volumes of mediodorsal lateral parvocellular, mediodorsal medial magnocellular and pulvinar anterior. **BD vs HC**: ↓ volumes in the mediodorsal medial magnocellular, lateral geniculate, medial geniculate and pulvinar anterior. **BD-I vs HC**: ↓ volumes in lateral geniculate nuclei, mediodorsal lateral parvocellular, mediodorsal medial magnocellular, medial geniculate nuclei and pulvinar anterior. **BD-II vs HC**: no significant differences.
Thiel et al., 2024	Cross-sectional	Germany	3	SPM12	MNI	sMRI [GMV] DTI [FA, MD, RD, AD]	Whole-brain	**BD-I vs BD-II**: GM: no significant differences. WM: ↓FA located in the forceps minor of the corpus callosum; ↑RD. MD and AD no significant differences. **BD-I vs HC**: GM: no significant differences. WM: ↓FA located in the forceps minor of

(*continued on next page*)

Table 2 (*continued*)

First author, study year	Study design	Country	Field strength (Tesla)	Imaging software	Space/Atlas	Type of MRI [main outcome (s)]	Whole brain/ROI	Main findings
								the corpus callosum, with almost all other major fiber tracts affected; ↑RD, ↑MD. AD no significant differences. **BD-II vs HC**: GM: no significant differences. WM: ↓FA in two small clusters in the left body of the CC.

Legend. BD-I, bipolar disorder type I; BD-II, bipolar disorder type II; HC, healthy controls; NA, not available; MDD, major depressive disorder; SCZ, schizophrenia; sMRI, structural magnetic resonance imaging; fMRI, functional magnetic resonance imaging; GM, gray matter; WM, white matter; ROI, region of interest; LV/C, lateral ventricle to cerebrum area ratio; CT, cortical thickness; VBM, voxel-based morphometry; FDR, False Discovery Rate; FA, fractional anisotropy; DTI, diffusion tensor imaging; ADC, apparent diffusion coefficient; DC, dorsal caudate; SA, surface area; WMH, white matter hyperintensities; MNI, Montreal Neurological Institute; TBV/ICV, ratio of total brain volume to intracranial volume; MD, mean diffusivity; VR, volume ratio; RD, radial diffusivity; AD, axial diffusivity; MO, mode; LGI, local gyrification index; ILF/FOF, inferior longitudinal fasciculus; SLF, superior longitudinal fasciculus; DLPFC, dorsolateral prefrontal cortex; VLPFC, ventrolateral prefrontal cortex; OFC, orbitofrontal cortex; RMFG, rostral middle frontal gyrus; dALFF, dynamic amplitude of low-frequency fluctuation; rSTG, right superior temporal gyrus; MTG, middle temporal gyrus; SMT, spherical mean technique; IASF, intra-axonal signal fraction; Dpar, axonal parallel diffusivity.

SCZ in the fronto-temporal and callosal networks. However, there were no significant differences in diffusion indices between BD and SCZ nor between BD-I (n = 18) and BD-II (*n* = 15) (Squarcina et al., 2017). Kieseppä et al. (2022), investigating DTI changes, found decreased FA, increased MD, and RD in the corpus callosum in BD-I but not in BD-II and MDD, with no significant diffusion index changes in BD-II compared to HC (Kieseppä et al., 2022).

Two studies (Caseras et al., 2015; Foley et al., 2018) focused on specific WM tracts. Foley et al. (2018) found lower FA in the left and right uncinate fasciculus in BD-I compared to BD-II and HC, with no difference between BD-II and HC. In addition, no significant differences among the three groups were observed in the cingulum body and parahippocampal cingulum (Foley et al., 2018). Similarly, Caseras et al. (2015) observed lower FA in the right uncinate fasciculus in patients with BD-I compared to BD-II and HC (Caseras et al., 2015). Moreover, Canales-Rodríguez et al. (2023) found no significant differences between BD subtypes in any of the four diffusion metrics analyzed, including FA, MD, intra-axonal signal fraction, and microscopic axonal parallel diffusivity derived from the spherical mean technique (Canales-Rodríguez et al., 2023). Lastly, Thiel et al. (2024) found that BD-I had lower FA values in widespread clusters, including almost all major projection, association, and commissural fiber tracts, compared with HC. Relative to BD-II, BD-I had lower FA, primarily in the anterior corpus callosum. BD-II exhibited significantly lower FA compared with HC in the left body of the corpus callosum (Thiel et al., 2024). Although no significant differences in AD values between groups emerged, BD-I displayed significantly higher RD values compared with BD-II and HC, and significantly higher MD compared with HC (Thiel et al., 2024).

Overall, while WM abnormalities in BD subtypes show heterogeneity and lack consistent replication, current evidence points toward a tendency for more disrupted WM microstructure in BD-I compared to BD-II.

3.3.2. White matter hyperintensities (WMH)

A prospective study investigating signal hyperintensities in three brain regions (periventricular WM, deep WM, and subcortical GM) among treatment-refractory patients with BD revealed that those with BD-I over age 30 had a significantly greater frequency of periventricular WMHs than HC and those with BD-II, with no significant differences between BD-II and HC (Altshuler et al., 1995). Kieseppä et al. (2022), investigating WMHs in BD and MDD, found that patients with BD-I showed deep WMHs mainly in the right frontal lobe, while patients with BD-II and MDD showed deep WMHs in the right and left frontal lobes and basal nuclei, and in the left frontal lobe, respectively (Kieseppä et al., 2022). Tighe et al. (2012) studied the effects of familiarity and psychosis on WMHs. They observed a linear trend of increase in the mean total WMH volume when comparing HC, unaffected relatives, patients with BD-II, and patients with BD-I with and without a history of psychotic symptoms (Tighe et al., 2012).

In summary, the included MRI investigations collectively highlight significant differences in WMHs between BD subtypes, primarily involving BD-I patients (Table 2).

3.4. Functional magnetic resonance imaging

Five fMRI studies were included in this review (Table 2). Growing evidence suggests that individuals with BD may be characterized by reward hypersensitivity (Alloy et al., 2016; Nusslock et al., 2019) and emotion dysregulation (Miola et al., 2022a; De Prisco et al., 2023). For this reason, Caseras et al. (2013, 2015) carried out two task-based investigations concerning reward anticipation and emotion regulation. During the reward anticipation task, Caseras et al. (2013) found that patients with BD-II showed greater bilateral ventral striatal activity than HC and BD-I. Interestingly, the authors evidenced that BD-II had significantly greater left putamen volume than BD-I, with the left putamen volume correlating positively with left ventral striatal activity to reward anticipation in all participants. They also conducted a whole-brain level analysis, which showed greater activity in the left ventrolateral prefrontal cortex, insula, precentral gyrus, and middle and superior temporal cortex of BD-II relative to BD-I and HC. BD-II also exhibited greater activity than HC in the caudate nuclei bilaterally and the left dorsolateral prefrontal cortex, while no significant differences emerged between BD-I and HC (Caseras et al., 2013).

The same research group performed a multimodal study that included anatomical diffusion weighted (see above) and an emotion regulation fMRI task in euthymic BD. Participants were administered a verbal working memory (*n*-back) task with emotional distractors with a focus on specific ROIs involved in cognitive (dorsolateral prefrontal cortex [DLPFC]) and emotional processing (amygdala, nucleus accumbens) (Caseras et al., 2015). At the behavioral level, at the highest working memory load, reaction times to targets were increased in BD-I compared to HC regardless of the presentation of distracters. At the neural level, patients showed differential responses based on the type of emotional distracters. Relative to HC and BD-II, the activation of DLPFC and limbic regions was increased when fear and happy distracters were

Table 3
Brain regions showing significant differences between BD-I and BD-II identified in structural, functional, and diffusion magnetic resonance imaging studies.

Brain areas	Author and year	Contrast	Sample size
Desikan–Killiany atlas sMRI			
Superior temporal gyrus left	Maller et al., 2014	BD-I < BD-II	BD-I: 16; BD-II: 15
Insula right	Woo et al., 2021	BD-I > BD-II	BD-I: 30; BD-II: 44
Medial orbitofrontal gyrus right	Maller et al., 2014	BD-I < BD-II	BD-I: 16; BD-II: 15
Temporal pole right	Abè et al. 2016	BD-I < BD-II	BD-I: 81; BD-II: 59
Desikan–Killiany atlas fMRI			
Caudal middle frontal gyrus left	Caseras et al., 2015	Fear distracters BD-I > BD-II Happy distracters BD-I < BD-II	BD-I: 16; BD-II: 19
Insula left	Caseras et al., 2013	BD-I < BD-II	BD-I: 17; BD-II: 15
Middle temporal gyrus left	Caseras et al., 2013	BD-I < BD-II	BD-I: 17; BD-II: 15
Pars opercularis left	Caseras et al., 2013	BD-I < BD-II	BD-I: 17; BD-II: 15
Pars orbitalis left	Caseras et al., 2013	BD-I < BD-II	BD-I: 17; BD-II: 15
Pars triangularis left	Caseras et al., 2013	BD-I < BD-II	BD-I: 17; BD-II: 15
Precentral gyrus left	Caseras et al., 2013	BD-I < BD-II	BD-I: 17; BD-II: 15
Rostral middle frontal gyrus left	Caseras et al., 2015	Fear distracters BD-I > BD-II Happy distracters BD-I < BD-II	BD-I: 16; BD-II: 19
Superior temporal gyrus left	Caseras et al., 2013	BD-I < BD-II	BD-I: 17; BD-II: 15
Caudal middle frontal gyrus right	Caseras et al., 2015	Fear distracters BD-I > BD-II Happy distracters BD-I < BD-II	BD-I: 16; BD-II: 19
Lateral orbitofrontal gyrus right	Wei et al., 2022	BD-I < BD-II	BD-I: 28; BD-II: 36
Medial orbitofrontal gyrus right	Wei et al., 2022	BD-I < BD-II	BD-I: 28; BD-II: 36
Middle temporal gyrus right	Liu et al., 2022	BD-I < BD-II	BD-I: 31; BD-II: 32
Rostral middle frontal gyrus right	Caseras et al., 2015	Fear distracters BD-I > BD-II Happy distracters BD-I < BD-II	BD-I: 16; BD-II: 19
Desikan–Killiany atlas DTI			
Caudal middle frontal gyrus left	Ha et al., 2011	BD-I < BD-II	BD-I: 12; BD-II: 12
Middle temporal gyrus left	Maller et al., 2014	BD-I > BD-II	BD-I: 16; BD-II: 15
Pars orbitalis left	Liu et al., 2010	BD-I > BD-II	BD-I: 14; BD-II: 13
Superior frontal gyrus left	Ha et al., 2011	BD-I < BD-II	BD-I: 12; BD-II: 12
Pars opercularis right	Liu et al., 2010	BD-I > BD-II	BD-I: 14; BD-II: 13
Pars orbitalis right	Liu et al., 2010	BD-I > BD-II	BD-I: 14; BD-II: 13
Pars triangularis right	Liu et al., 2010	BD-I > BD-II	BD-I: 14; BD-II: 13
Postcentral gyrus right	Ha et al., 2011	BD-I < BD-II	BD-I: 12; BD-II: 12
Precuneus right	Liu et al., 2010	BD-I > BD-II	BD-I: 14; BD-II: 13
Caudal middle frontal gyrus right	Ha et al., 2011	BD-I < BD-II	BD-I: 12; BD-II: 12
Subcortical sMRI			
Hippocampus left	Cao et al., 2017	BD-I < BD-II	NR
Putamen left	Caseras et al., 2013	BD-I < BD-II	BD-I: 17; BD-II: 15
Hippocampus right	Cao et al., 2017	BD-I < BD-II	NR
Subcortical fMRI			
Amygdala left	Caseras et al., 2015	BD-I > BD-II	BD-I: 16; BD-II: 19
Caudate left	Caseras et al., 2013	BD-I < BD-II	BD-I: 17; BD-II: 15
Pallidum left	Caseras et al., 2013	BD-I < BD-II	BD-I: 17; BD-II: 15
Putamen left	Caseras et al., 2013	BD-I < BD-II	BD-I: 17; BD-II: 15
Thalamus proper left	Mørch-Johnsen et al., 2023	BD-I < BD-II	BD-I: 183; BD-II: 125
Amygdala right	Caseras et al., 2015	BD-I > BD-II	BD-I: 16; BD-II: 19
Caudate right	Caseras et al., 2013	BD-I < BD-II	BD-I: 17; BD-II: 15
Pallidum right	Caseras et al., 2013	BD-I < BD-II	BD-I: 17; BD-II: 15
Putamen right	Caseras et al., 2013	BD-I < BD-II	BD-I: 17; BD-II: 15
Subcortical DTI			
Putamen left	Maller et al., 2014	BD-I > BD-II	BD-I: 16; BD-II: 15
John Hopkins University DTI-based white matter atlas			
Anterior thalamic radiation right	Maller et al., 2014	BD-I > BD-II	BD-I: 16; BD-II: 15
Anterior thalamic radiation left	Maller et al., 2014	BD-I > BD-II	BD-I: 16; BD-II: 15
Forceps minor center	Thiel et al., 2024	BD-I < BD-II	BD-I: 73; BD-II: 63
Inferior fronto-occipital fasciculus left	Maller et al., 2014	BD-I > BD-II	BD-I: 16; BD-II: 15
Inferior longitudinal fasciculus right	Ambrosi et al., 2016 Ha et al., 2011	BD-I > BD-II BD-I < BD-II	BD-I: 25; BD-II: 25 BD-I: 12; BD-II: 12
Inferior longitudinal fasciculus left	Maller et al., 2014	BD-I > BD-II	BD-I: 16; BD-II: 15
Superior longitudinal fasciculus left	Maller et al., 2014	BD-I > BD-II	BD-I: 16; BD-II: 15
Uncinate fasciculus left	Foley et al., 2018	BD-I < BD-II	BD-I: 32; BD-II: 34
Uncinate fasciculus right	Caseras et al., 2015 Foley et al., 2018	BD-I < BD-II BD-I < BD-II	BD-I: 16; BD-II: 19 BD-I: 32; BD-II: 34

BD-I, bipolar disorder type I; BD-II, bipolar disorder type II; DTI, diffusion tensor imaging; fMRI, functional magnetic resonance imaging; NR, not reported; sMRI, structural magnetic resonance imaging.

presented in BD-I. Furthermore, when neutral distracters were shown, the activation in the DLPFC was reduced, and that of the limbic regions was increased in BD-I compared to HC. Relative to HC and BD-I, the activation of DLPFC and amygdala was increased when fear distracters were presented in BD-II. The negative DLPFC-amygdala connectivity was increased in BD-II when fear distracters were presented compared to BD-I and HC (Caseras et al., 2015).

Two rs-fMRI studies used seed-based FC analyses to investigate intrinsic connectivity of cerebellum (Olivito et al., 2022b) and caudate (Wei et al., 2022), two critical regions involved in motor, cognitive, and emotional regulation in BD patients (Blumberg et al., 2000; Cui et al., 2022; Ahmed et al., 2023; Tai et al., 2024). Wei et al. (2022) performed a dorsal caudate-seeded FC study revealing that BD-I had significantly decreased FC between the caudate and the orbitofrontal cortex as compared to BD-II, and between the caudate and the putamen and

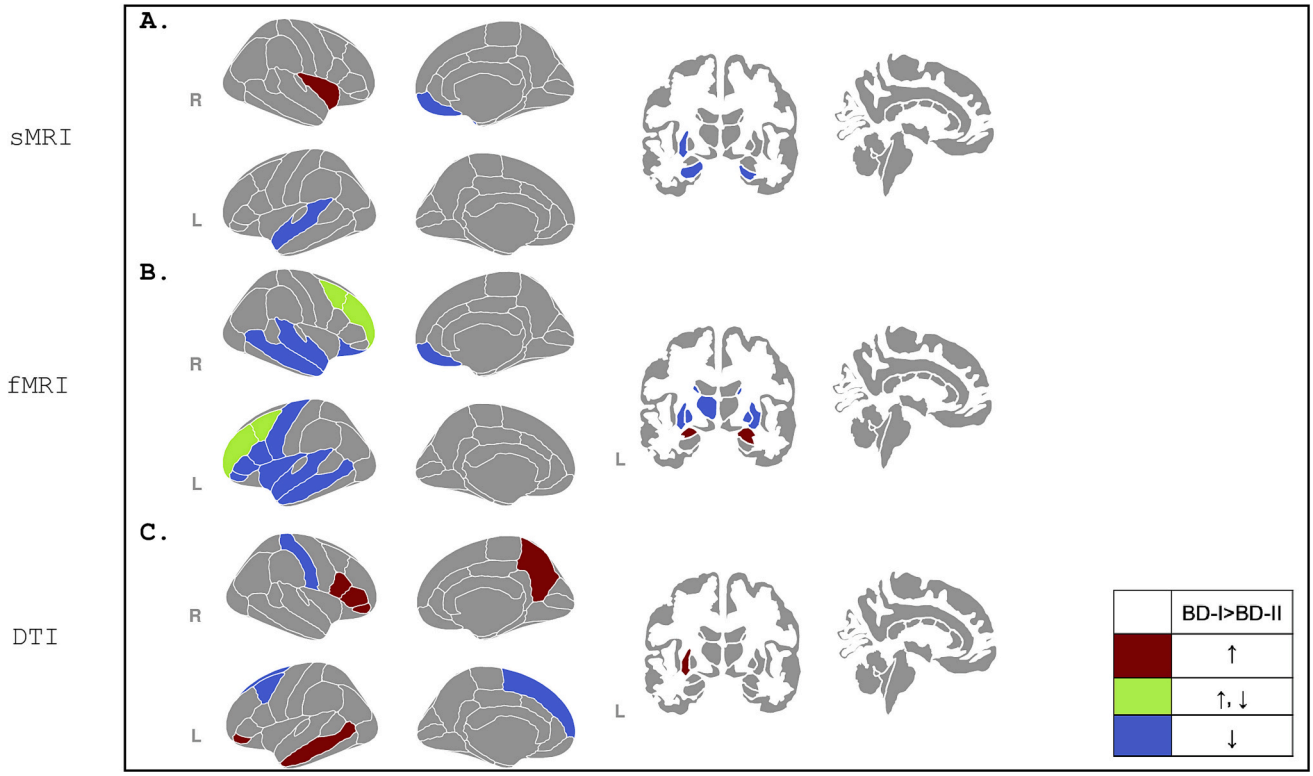


Fig. 2. Neuroimaging differences between BD-I and BD-II. Findings from structural magnetic resonance imaging (A), functional magnetic resonance imaging (B), and diffusion tensor imaging (C) studies are displayed on the Desikan–Killiany atlas. The medial and lateral cortical surfaces are displayed for each hemisphere on the left part, the subcortical regions in the center, and the colorbar on the right part of each panel, respectively. The color bar code indicates whether one study reported greater (↑), smaller (↓) or bidirectional (↑,↓) imaging index changes in BD-I compared to BD-II. L, left hemisphere; R, right hemisphere. The renderings were created using the R-package *ggseg*.

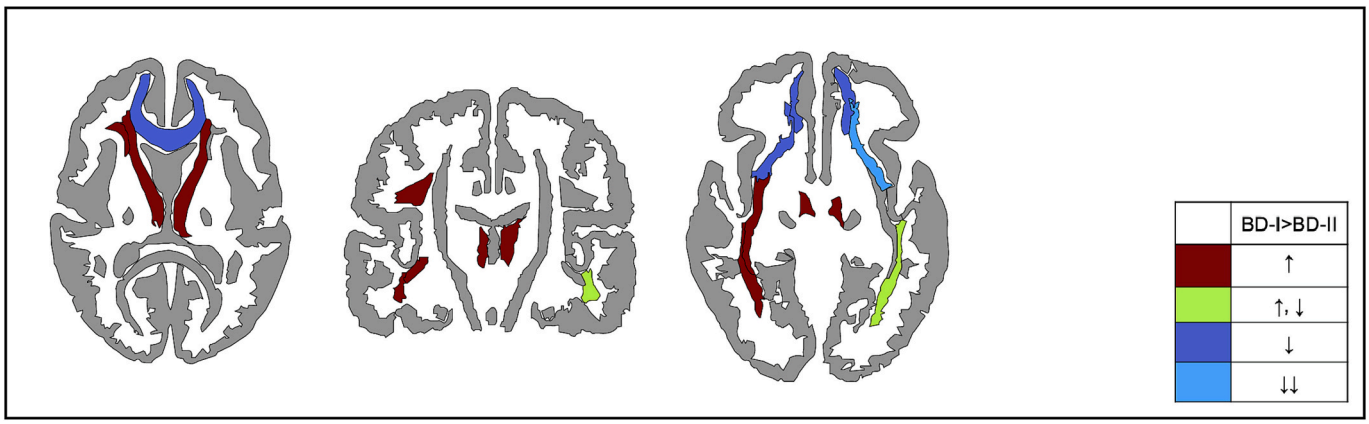


Fig. 3. White matter tract differences between BD-I and BD-II. Findings from probabilistic tractography studies are displayed in the upper coronal (left), axial (center), and lower (right) coronal projections on the Johns Hopkins University DTI-based white matter atlas. The color bar code indicates whether one study reported greater (↑), smaller (↓), bidirectional (↑,↓), or two studies smaller (↓↓) connectivity in BD-I compared to BD-II. L, left hemisphere; R, right hemisphere. The renderings were created using the R-package *ggseg*.

parahippocampal gyrus as compared with HC. BD-II exhibited decreased FC between the caudate and the orbitofrontal cortex, ventrolateral prefrontal cortex, dorsolateral prefrontal cortex, posterior parietal cortex, inferior temporal gyrus, parahippocampal gyrus, supplementary motor area, thalamus, pons, and cerebellum as compared with the HC group (Wei et al., 2022). Finally, Olivito et al. (2022b), exploring the cerebellar-cerebral FC, found an altered pattern of cerebellar-cerebral FC involving both left and right dentate nuclei in the BD groups compared with HC. Nonetheless, no significant FC differences were found between BD-I and BD-II (Olivito et al., 2022b) (see Table 2 for further details). Although in these studies, brain activity and connectivity were considered to be static, recent research has shown that intrinsic fluctuations also vary over time, and this is associated with brain function (Cattarinussi et al., 2023a). Consistent with this, Liu et al. (2022) investigated the dynamic-ALFF (dALFF) in BD and found a widespread decrease in dALFF values compared with HCs, mainly in the frontal, parietal, and temporal cortices. Of note, a significant reduction in dALFFs was present in the right superior and middle temporal gyrus in BD-I compared to BD-II (Liu et al., 2022).

4. Discussion

To our knowledge, this is the first systematic review to examine differences in structural and functional MRI measures in BD-I and BD-II. In this review, we included 38 MRI studies and 41 experiments. Five of these were fMRI studies, while the remaining 33 were structural MRI studies. Among the structural studies, nine assessed WM microstructural abnormalities, three investigated WMHs, and the others conducted voxel-based or surface-based analyses of GM alterations. Based on the overall mean score, 89.5 % of the included studies were rated as high quality (Table 1).

Although the high methodological and clinical heterogeneity across included neuroimaging studies limits the certainty of conclusions, several noteworthy findings emerged. First, structural ROI-based and whole-brain MRI studies yielded spatially heterogeneous changes in BD, with GM volume reductions mainly driven by BD-I. Second, a generally widespread decrease in CT was found in BD, with thinner cortical regions in BD-I than in BD-II. Third, specific WM differences between BD-I and BD-II remain inconclusive; only WMHs were more frequently present in BD-I. Fourth, fMRI studies revealed significant differences between BD subtypes in task-based and resting-state studies, with increased limbic activation during emotional processing and reduced cortico-striatal connectivity, which was greater in BD-I than BD-II.

Structural MRI studies investigated specific ROIs for which there was a strong a priori hypothesis, as well as the whole brain, revealing mixed results in different brain regions. Although most ROI-based investigations focused on temporal and frontal structures, they found no volumetric differences between BD subtypes (Brambilla et al., 2003; Gutiérrez-Galve et al., 2012; Yang et al., 2021). Of note, these studies aimed at identifying structural differences in BD may be underpowered to investigate differences within BD subtypes (Brambilla et al., 2003). In addition, the hippocampus, amygdala, basal ganglia, thalamic nuclei, and cerebellar structures have also been investigated. Regarding the hippocampus, both Janiri et al., 2019, Haukvik et al., 2022, and Cao et al., 2017 did not reveal consistent differences between BD-I and BD-II, although both BD subtypes exhibited lower hippocampal volumes, and this difference seemed to be primarily driven by the BD-I subgroup (Cao et al., 2017; Haukvik et al., 2022). This suggests hippocampal volume reductions might be a common feature in BD and may not be a differentiating biomarker between the BD subtypes. In addition, GM volume reductions in the left hippocampus are shared across patients with BD, MDD, SCZ, and schizoaffective disorder (Brosch et al., 2022). Similarly, Brambilla et al. (2003) found a significantly larger amygdala in BD. Conversely, no difference was found in basal ganglia volume in BD in a single study with a small sample (Brambilla et al., 2001). Investigating distinct nuclei of the thalamus, patients with BD and SCZ spectrum disorders had smaller medial and posterior thalamic nuclei volumes, and this result was driven by BD-I (Mørch-Johnsen et al., 2023). Additionally, mediodorsal lateral parvocellular, mediodorsal medial magnocellular, and pulvinar anterior nuclei volume were reduced in BD-I compared with BD-II (Mørch-Johnsen et al., 2023). These findings suggest that the neurobiology of BD-I may lie closer to SCZ spectrum disorders on a continuum of illness, aligning with insights from prior genetic research (Almeida et al., 2020). Regarding the cerebellum, a reduction in cerebellar volume emerged in both BD subtypes (Kim et al., 2020; Olivito et al., 2022a), with a more diffuse involvement in BD-II (Olivito et al., 2022a). Furthermore, larger lateral ventricles have been found in BD-I, also when compared to BD-II (Hauser et al., 2000), an unspecific finding that was previously reported in other major psychiatric disorders, especially in SCZ (Chance et al., 2003; Horga et al., 2011; Svancer and Spaniel, 2021). Whole brain morphometric investigations yielded heterogeneous findings (Ha et al., 2009; Caseras et al., 2013; Miola et al., 2022c) and were not consistently replicated across the studies (Maller et al., 2014, 2015). BD-I presented widespread GM volume reductions in the bilateral frontal, temporal, parietal, and parahippocampal cortices and in the right middle and inferior occipital gyrus (Ha et al., 2009; Miola et al., 2022c). On the other hand, both BD-II and BD-I showed GM deficits in the ventromedial prefrontal regions (Ha et al., 2009), and BD-II exhibited significantly greater left putamen volume compared to BD-I (Caseras et al., 2013). Additionally, this volume increase in the left putamen positively correlated with left ventral striatal activity during reward anticipation tasks (Caseras et al., 2013). This finding might imply potential differences in the neural mechanisms underlying reward processing in the BD subtypes.

Most surface-based studies showed reduced CT in BD, and lower CT was more frequently observed in BD-I than BD-II (Lyoo et al., 2006; Abé et al., 2016, 2022; Hibar et al., 2018; Woo et al., 2021; McWhinney et al., 2022). BD-I and BD-II displayed similar cortical abnormalities, including lower volume, CT, and surface area in frontal regions but not in temporal regions, where only BD-I had reduced cortical volume and CT (Abé et al., 2016). In addition, BD-I showed lower CT relative to BD-II in the ventral prefrontal cortex, including the ventrolateral prefrontal cortex and the orbitofrontal cortex (Woo et al., 2021). Of note, positive correlations between executive function performance and CT in the medial prefrontal cortex were found in BD-II but not in BD-I. Thus, the functional relevance of CT may differ regionally between BD subtypes (Abé et al., 2018). CT differences between BD subtypes have also been reported in limbic regions (Abé et al., 2022) and SA differences in the right long insular gyrus (Woo et al., 2021), although negative findings for CT and surface area between BD subtypes have been reported (Lyoo et al., 2006; Hibar et al., 2018; Matsumoto et al., 2023). In addition, all cerebellar subregions showed an increased CT in BD (Kim et al., 2020), with no significant differences between BD-I and BD-II (Kim et al., 2020). Similar to the hippocampus, cerebellar volume reductions and increased CT of all cerebellar subregions observed in BD may represent common features to both BD subtypes, warranting additional exploration. These findings indicate that patients with BD-I are characterized by lower CT compared to BD-II, mainly in the prefrontal, temporal, and limbic regions. This may suggest that BD-I and BD-II present different neurodevelopmental mechanisms that result in different cortical abnormalities. This hypothesis aligns with genome-wide association studies showing genetic heterogeneity between BD subtypes (Charney et al., 2017). We might speculate that genetic differences between the two disorders underlie differential neurodevelopmental processes in the two groups of BD patients, ultimately leading to disorder-specific patterns of cortical alterations.

WM findings showed a large heterogeneity, probably due to differences in DTI measures and brain regions studied, with most studies suggesting a more severe disruption of WM microstructure in BD-I compared to BD-II. Mixed findings for comparing BD subtypes were reported for the FA in the right inferior longitudinal fasciculus (Ha et al., 2011; Ambrosi et al., 2016). Increased FA values have been reported in the right precuneus, right inferior frontal gyrus, and left inferior prefrontal area in BD-I compared to BD-II (Liu et al., 2010). Additionally, two studies on specific WM tracts showed decreased FA in the uncinate fasciculus in BD-I compared to BD-II (Caseras et al., 2015; Foley et al., 2018). This is consistent with previous research on this tract in BD-I (Versace et al., 2008; Sussmann et al., 2009; Lin et al., 2011). Notably, the uncinate fasciculus has been highlighted as a key WM tract for top-down emotion regulation by carrying connections from the prefrontal cortex to regions of the temporal lobe, including the amygdala (d'Arbeloff et al., 2018; Pedersen et al., 2022). This finding further supports that abnormalities in emotion regulation circuits are predominant in BD-I relative to BD-II. Although the conclusions from these studies remain tentative due to consistently small sample sizes and varying methodologies, a recent study by Thiel et al. (2024) found lower FA, primarily in the anterior corpus callosum in BD-I compared with BD-II, indicating greater WM disruption. This distinction was further reflected by the extent of impairment compared to HC. BD-I showed widespread WM reductions, affecting all major projection, association, and commissural fiber tracts, including the corpus callosum. In contrast, BD-II had lower FA in the left body of the corpus callosum (Thiel et al.,

2024). The reduction of FA in the corpus callosum across both BD subtypes aligns with prior research identifying this as one of the most consistent effects in BD (Favre et al., 2019; Yang et al., 2019; Thiel et al., 2023). The corpus callosum plays a crucial role in interhemispheric integration, and reduced WM integrity in the corpus callosum has been found across severe mental disorders (MDD, BD, and SCZ), supporting that disruptions in interhemispheric WM connectivity may represent a common pathophysiological pathway and may contribute to cognitive and emotional deficits (Wise et al., 2017; Cui et al., 2020; Koshiyama et al., 2020; Meinert et al., 2022; Videtta et al., 2023). Consistently, decreased FA and increased diffusivity indices were found in BD-I, BD-II, and SCZ, with overlapping affected areas spanning the frontotemporal and callosal networks (Squarcina et al., 2017), suggesting that these WM abnormalities may represent common features of the BD-SCZ spectrum. Relative to BD-II, BD-I showed an increase in MD in the brainstem, internal capsule, middle temporal gyrus, putamen, and thalamic radiation (Maller et al., 2014), in RD, in the insula (Maller et al., 2014), and ADC, in the left frontal, right parietal, temporal regions, and right thalamus, respectively (Ha et al., 2011).

When considering the WMHs, lesions associated with vascular insults to the brain, and related to cognitive decline (Chen et al., 2021b), several studies showed an increased prevalence in BD-I. Adult BD-I showed a significantly greater frequency of periventricular WMHs than BD-II (Altshuler et al., 1995). In addition, WMH volume was increased with a linear trend in unaffected relatives of patients with BD, BD-II, and BD-I without and with a history of psychosis (Tighe et al., 2012), thus suggesting their role as markers of disease burden in BD-I and further supporting the bipolar spectrum. Interestingly, BD-II showed a WMHs pattern more similar to MDD than BD-I (Kieseppä et al., 2022), which supports the concept of a continuum of the "manic-depressive illness".

FMRI studies provided helpful insight into differences in functional connectivity and activation patterns in BD subtypes. Patients with BD-I displayed abnormalities in activation and structural and functional connectivity between the prefrontal cortex and subcortical structures during emotion regulation, whereas such deficits did not extend to BD-II (Caseras et al., 2013, 2015). These findings, along with altered WM microstructure organization in the right uncinate fasciculus in patients with BD-I compared with BD-II, support crucial differences in the pathophysiology of BD subtypes and suggest an inefficient coupling between prefrontal cortical areas and emotion regulation circuitry, with an altered dorsolateral prefrontal cortex downregulation of amygdala reactivity in BD-I but not in BD-II. Notably, cortico-limbic functional abnormalities have also been reported in unaffected relatives of BD, suggesting their candidate role as an endophenotype of the disorder (Cattarinussi et al., 2019, 2022, 2023b). In addition, previous reviews revealed altered cortico-limbic circuits and amygdala reactivity as underlying mechanisms of impairment of emotional perception in BD-I (Bi et al., 2022; Bigot et al., 2020). Such results align with previous studies showing an altered emotion processing in BD in behavioral tasks, even during remission, with worse performance in BD-I relative to BD-II (Bozikas et al., 2006; Caseras et al., 2015; Miola et al., 2023c). These results are also consistent with worse social cognition in BD-I than BD-II (Dell'Osso et al., 2017), which may impair interpersonal relationships and global functioning.

Functional connectivity at rest showed a pattern of neural disconnection in BD, which seemed greater in BD-I than in BD-II. In particular, BD-I had a decreased FC between the dorsal caudate and the putamen and the parahippocampal gyrus compared to HC and a lower FC than those with BD-II between the DC and the orbitofrontal cortex (Wei et al., 2022); notably, the orbitofrontal cortex plays a role in decision making for emotional and reward-related behaviors (Kringelbach, 2005). Moreover, cerebello-cortical FC, which has been associated with the onset of manic symptoms (Lupo et al., 2018), was altered in the dentate-cortical connections in BD with no difference between BD subtypes (Olivito et al., 2022b). More recently, dynamic resting-state abnormalities have been reported in BD, and they seem to be associated with the severity of affective symptoms (Cattarinussi et al., 2023a). BD-I and BD-II showed a significant decrease in dALFF in frontal, parietal, occipital, and temporal cortices and the limbic system. In addition, relative to BD-II, BD-I had reduced dALFF in the right superior and middle temporal gyrus (Liu et al., 2022), which are involved in emotion regulation (Patel et al., 2023). These findings suggest dALFF as a putative resting-state index marker that may contribute to differentiating BD-I and BD-II.

Medication exposure (Ilzarbe and Vieta, 2023), along with psychiatric and medical comorbidities and illness severity, may represent important potential confounding factors in the included studies. Baseline clinical scales were generally within the mild or euthymic range, consistent with recruitment outside acute episodes (Table 1). Some included studies showed that participants with BD-II exhibited higher depressive symptom burden compared to those with BD-I (e.g., Ha et al., 2009; Liu et al., 2010; Ambrosi et al., 2016; Kieseppä et al., 2022; Woo et al., 2021), whereas (hypo)manic symptom scores were overall low and comparable between the diagnostic groups.

The majority of participants were receiving psychotropic treatment at the time of the MRI scan, with combinations of mood stabilizers, antidepressants, antipsychotics, and benzodiazepines being common in individuals with BD-I and BD-II (eTable3). In some studies, patients with BD-I were more frequently treated with mood stabilizers and antipsychotics, whereas those with BD-II showed greater exposure to antidepressants (Abé et al., 2016; Foley et al., 2018; Liu et al., 2022; Miola et al., 2022c; Wei et al., 2022; Thiel et al., 2024), consistent with clinical prescription patterns in major mood disorders (Hernandorena et al., 2025). Independent of BD subtype-specific prescription patterns, previous reviews support a normalising effect of psychotropic medications, particularly lithium and mood stabilizers, on brain structure and function in individuals with BD (Hafeman et al., 2012; McDonald, 2015). Several included studies have investigated whether pharmacological profiles could explain brain differences between BD subtypes. While some investigations found no significant associations between medication use and neuroimaging findings (Altshuler et al., 1995; Brambilla et al., 2001, 2003; Lyoo et al., 2006; Ha et al., 2009; Caseras et al., 2013, 2015; Maller et al., 2015; Janiri et al., 2019; Choi et al., 2022; Liu et al., 2022; McWhinney et al., 2022; Miola et al., 2022c), other MRI studies suggested that specific treatments—particularly lithium, anticonvulsants, and antipsychotics—may exert measurable effects on brain morphology (Abé et al., 2016; Foley et al., 2018; Hibar et al., 2018; Woo et al., 2021; Abé et al., 2022; Haukvik et al., 2022; Canales-Rodríguez et al., 2023). Lithium exposure has been associated with greater WM integrity (higher FA) in the left uncinate fasciculus, thalamus, brainstem, and superior longitudinal fasciculus, as well as increased CT and GM volumes, especially in the hippocampus and occipital areas (Abé et al., 2016; Foley et al., 2018; Hibar et al., 2018; Haukvik et al., 2022; Canales-Rodríguez et al., 2023), whereas antipsychotics have shown the opposite trend (Hibar et al., 2018; Woo et al., 2021; Abé et al., 2022; Haukvik et al., 2022; Canales-Rodríguez et al., 2023). These findings align with previous MRI investigations showing that lithium may increase GM volume, specifically in the limbic system, thalamus, and amygdala (Savitz et al., 2010; Hibar et al., 2016; Sani et al., 2018), whereas antipsychotic exposure has been associated with smaller brain volumes (Abramovic et al., 2016). Most studies did not report current dose regimens, treatment duration, prior medication exposure, or specific drug combinations; thus, it remains unclear to what extent the observed effects reflect the illness itself, pharmacological treatment, or their interaction. Future investigations, including drug-free or, ideally, drug-naïve patients and employing prospective longitudinal designs with standardized medication characterization, are essential to disentangle illness- from treatment-related effects.

Although some studies excluded participants with comorbid psychiatric disorders (Brambilla et al., 2001, 2003; Lyoo et al., 2006; Gutiérrez-Galve et al., 2012; Caseras et al., 2013, 2015; Maller et al.,

2014, 2015; Ambrosi et al., 2016; Squarcina et al., 2017; Kim et al., 2020; Woo et al., 2021; Yang et al., 2021; Choi et al., 2022; Olivito et al., 2022a, 2022b; Wei et al., 2022), alcohol/substance abuse and/or major medical conditions (Brambilla et al., 2001, 2003; Ha et al., 2009, 2011; Gutiérrez-Galve et al., 2012; Caseras et al., 2013, 2015; Maller et al., 2014, 2015; Ambrosi et al., 2016; Cao et al., 2017; Squarcina et al., 2017; Foley et al., 2018; Janiri et al., 2019; Kim et al., 2020; Kieseppä et al., 2022; Woo et al., 2021; Yang et al., 2021; Choi et al., 2022; Liu et al., 2022; Miola et al., 2022c; Olivito et al., 2022a, 2022b; Wei et al., 2022; Canales-Rodríguez et al., 2023; Thiel et al., 2024), psychiatric and medical comorbidities were not systematically assessed across BD subtypes, nor were their potential effects on neuroimaging findings explored, representing another potential source of confounding. Indeed, individuals with BD frequently present with co-occurring physical disorders, including obesity, insulin resistance, and type 2 diabetes (Vancampfort et al., 2015; Miola et al., 2022d), as well as co-occurring psychiatric conditions such as substance use disorders, anxiety, ADHD, and personality disorders (Hunt et al., 2016; Preti et al., 2016, 2018; Schiweck et al., 2021). For example, obesity increases the likelihood of having low CT and may explain differences in cortical measures and subcortical brain volumes in people with BD (McWhinney et al., 2021, 2022), with higher BMI values being associated with GM and WM reductions in the emotion-generating and -regulating regions in individuals with first-episode mania (Bond et al., 2014). Of note, individuals with BD-II show more frequent co-occurring psychiatric diagnoses than those with BD-I (Hernandorena et al., 2023), especially anxiety disorders, eating disorders, and personality disorders (Dell'Osso et al., 2015; Karanti et al., 2020). Medical and psychiatric comorbidities may influence brain structure and function, contributing to the heterogeneity of neuroimaging findings.

Other factors may underlie the inconsistency in replicating structural and functional neuroimaging findings across BD subtypes. First, manic-depressive illness is a highly heterogeneous condition with different clinical sub-phenotypes (Coombes et al., 2020). Patients with BD can differ in variables associated with illness course, including the age of the first symptoms and the incident case of (hypo)mania, the duration of affective episodes, the stage of the illness, illness severity, and cognitive impairment, which are not reported systematically across the included studies. Second, variability in mood state at the time of neuroimaging assessments may limit the comparability of some of the included MRI investigations. Third, the cross-sectional design of most of the examined MRI studies limits the ability to make causal inferences and the generalizability of present findings (Vieta and De Prisco, 2024). Fourth, a limited sample size may result in insufficient statistical power to detect significant differences among BD subtypes (De Prisco and Vieta, 2024). Moreover, for each metric, the limited number of ROI-based studies and the number of whole-brain studies being below the minimum recommended to ensure adequate power and prevent results from being driven by single experiments (Müller et al., 2018) precluded a meta-analysis of the present findings. Finally, MRI scanning methods presented high heterogeneity, including scanning parameters, statistical approaches, and analysis pipelines.

Although neuroimaging differences exist between BD-I and BD-II, the existing literature remains limited, making it difficult to determine whether these differences are substantial or whether they reflect a continuum between the two BD subtypes. The neuroprogressive evolution of the disease may influence this continuum (Chen et al., 2021a), leading to complex alterations in brain structure and function over time. Integrating comprehensive clinical phenotyping, staging, and neuroimaging measures is crucial for improving within-group homogeneity, refining diagnostic accuracy, and tailoring therapeutic strategies for individuals with BD.

In conclusion, structural and functional neuroimaging studies can shed light on the neuroimaging features of BD subtypes, providing valuable insights into their underlying neural mechanisms. Structural MRI highlighted widespread variations in brain morphometry and surface characteristics, mainly driven by BD-I, possibly suggesting different neurodevelopmental pathways, although the findings were inconsistent across brain regions. WM alterations were also observed, but the specific differences between BD-I and BD-II remain inconclusive. Lastly, fMRI studies pointed to cortico-limbic disconnection in the BD subtypes, mostly in BD-I, in emotion regulation and reward processing. The neural signatures of BD subtypes appear to be related to neural networks rather than individual brain regions. Overall, these findings may contribute to refining our understanding of the neurobiological underpinnings of BD-I and BD-II and highlight potential avenues for integrating clinical phenotyping and providing targeted interventions.

CRediT authorship contribution statement

Alessandro Miola: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Data curation, Conceptualization. **Margherita Salvucci:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Data curation, Conceptualization. **Nicola Meda:** Writing – review & editing, Writing – original draft, Investigation, Data curation. **Giulia Cattarinussi:** Writing – review & editing, Writing – original draft, Investigation, Data curation. **Maria Lavinia Loré:** Writing – review & editing, Writing – original draft, Investigation, Data curation. **Niccolò Ghiotto:** Writing – review & editing, Writing – original draft, Investigation, Data curation. **Enrico Collantoni:** Writing – review & editing, Methodology. **Tommaso Boldrini:** Writing – review & editing, Methodology. **Nicolas A. Nunez:** Writing – review & editing, Methodology. **Mete Ercis:** Writing – review & editing, Methodology. **Michele De Prisco:** Writing – review & editing, Methodology. **Michele Fornaro:** Writing – review & editing, Supervision. **Marco Solmi:** Writing – review & editing, Supervision. **Marin Veldic:** Writing – review & editing, Supervision. **Joaquim Radua:** Writing – review & editing, Supervision. **Eduard Vieta:** Writing – review & editing, Supervision. **Mark A. Frye:** Writing – review & editing, Supervision. **Fabio Sambataro:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Data curation, Conceptualization.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

AM, MS, NM, GC, MLL, NG, EC, TB, NAN, ME, MDP, MF, MV, FS have no conflict of interest to declare.

MS received honoraria/has been a consultant for AbbVie, Angelini, Bausch Health, Boehringer Ingelheim, Lundbeck, Otsuka. EV has received grants and served as consultant, advisor or CME speaker for the following entities: ABBiotics, AbbVie, Adamed, Angelini, Biogen, Beckley-Psytech, Biohaven, Boehringer-Ingelheim, Celon Pharma, Compass, Dainippon Sumitomo Pharma, Ethypharm, Ferrer, Gedeon Richter, GH Research, Glaxo-Smith Kline, HMNC, Idorsia, Johnson & Johnson, Lundbeck, Luye Pharma, Medincell, Merck, Newron, Novartis, Orion Corporation, Organon, Otsuka, Roche, Rovi, Sage, Sanofi-Aventis, Sunovion, Takeda, Teva, and Viatris, outside the submitted work. MAF received grant support from Assurex Health and Mayo Foundation, received CME travel and honoraria from Carnot Laboratories and American Physician Institute, and has Financial Interest/Stock ownership/Royalties from Chymia LLC. JR has received CME honoraria from Inspira Networks for a machine learning course promoted by Adamed.

Acknowledgments

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2025.120605.

Data availability

Data that support the findings of this study are available on reasonable request from the corresponding author.

References

Abé, C., Ekman, C.-J., Sellgren, C., Petrovic, P., Ingvar, M., Landén, M., 2016. Cortical thickness, volume and surface area in patients with bipolar disorder types I and II. J. Psychiatry Neurosci. 41, 240–250. https://doi.org/10.1503/jpn.150093.

Abé, C., Rolstad, S., Petrovic, P., Ekman, C.-J., Sparding, T., Ingvar, M., Landén, M., 2018. Bipolar disorder type I and II show distinct relationships between cortical thickness and executive function. Acta Psychiatr. Scand. 138, 325–335. https://doi.org/10.1111/acps.12922.

Abé, C., Ching, C.R.K., Liberg, B., Lebedev, A.V., Agartz, I., Akudjedu, T.N., Alda, M., Alnæs, D., Alonso-Lana, S., Benedetti, F., Berk, M., Bøen, E., Bonnin, C. del M., Breuer, F., Brosch, K., Brouwer, R.M., Canales-Rodríguez, E.J., Cannon, D.M., Chye, Y., Dahl, A., Dandash, O., Dannlowski, U., Dohm, K., Elvsåshagen, T., Fisch, L., Fullerton, J.M., Goikolea, J.M., Grotegerd, D., Haatveit, B., Hahn, T., Hajek, T., Heindel, W., Ingvar, M., Sim, K., Kircher, T.T.J., Lenroot, R.K., Malt, U.F., McDonald, C., McWhinney, S.R., Melle, I., Meller, T., Melloni, E.M.T., Mitchell, P.B., Nabulsi, L., Nenadić, I., Opel, N., Overs, B.J., Panicalli, F., Pfarr, J.-K., Poletti, S., Pomarol-Clotet, E., Radua, J., Repple, J., Ringwald, K.G., Roberts, G., Rodriguez-Cano, E., Salvador, R., Sarink, K., Sarró, S., Schmitt, S., Stein, F., Suo, C., Thomopoulos, S.I., Tronchin, G., Vieta, E., Westlye, L.T., White, A.G., Yatham, L.N., Zak, N., Thompson, P.M., Andreassen, O.A., Landén, M., 2022. Longitudinal structural brain changes in bipolar disorder: a multicenter neuroimaging study of 1232 individuals by the ENIGMA bipolar disorder working group. Biol. Psychiatry 91, 582–592. https://doi.org/10.1016/j.biopsych.2021.09.008.

Abramovic, L., Boks, M.P., Vreeker, A., Bouter, D.C., Kruiper, C., Verkooijen, S., van Bergen, A.H., Ophoff, R.A., Kahn, R.S., van Haren, N.E., 2016. The association of antipsychotic medication and lithium with brain measures in patients with bipolar disorder. Eur. Neuropsychopharmacol. 26, 1741–1751. https://doi.org/10.1016/j.euroneuro.2016.09.371.

Ahmed, Y.B., Al-Bzour, A.N., Alzghoul, S.M., Ibrahim, R.B., Al-Khalili, A.A., Al-Majali, G. N., Hamza, A.I., Al-Zamer, Y.S., Alhayek, K., Kofahi, R., Leffler, A., El Salem, K., Al Qawasmeh, M., 2023. Limbic and cortical regions as functional biomarkers associated with emotion regulation in bipolar disorder: a meta-analysis of neuroimaging studies. J. Affect. Disord. 323, 506–513. https://doi.org/10.1016/j.jad.2022.11.071.

Al-Arfaj, H.K., Al-Sharydah, A.M., AlSuhaibani, S.S., Alaqeel, S., Yousry, T., 2023. Task-based and resting-state functional MRI in observing eloquent cerebral areas personalized for epilepsy and surgical oncology patients: a review of the current evidence. J. Pers. Med. 13, 370. https://doi.org/10.3390/jpm13020370.

Alexander, A.L., Lee, J.E., Lazar, M., Field, A.S., 2007. Diffusion tensor imaging of the brain. Neurotherapeutics 4, 316–329. https://doi.org/10.1016/j.nurt.2007.05.011.

Alloy, L.B., Olino, T., Freed, R.D., Nusslock, R., 2016. Role of reward sensitivity and processing in major depressive and bipolar spectrum disorders. Behav. Ther. 47, 600–621. https://doi.org/10.1016/j.beth.2016.02.014.

Almeida, H.S., Mitjans, M., Arias, B., Vieta, E., Ríos, J., Benabarre, A., 2020. Genetic differences between bipolar disorder subtypes: a systematic review focused in bipolar disorder type II. Neurosci. Biobehav. Rev. 118, 623–630. https://doi.org/10.1016/j.neubiorev.2020.07.033.

Altshuler, L.L., Curran, J.G., Hauser, P., Mintz, J., Denicoff, K., Post, R., 1995. T2 hyperintensities in bipolar disorder: magnetic resonance imaging comparison and literature meta-analysis. Am. J. Psychiatry 152, 1139–1144. https://doi.org/10.1176/ajp.152.8.1139.

Ambrosi, E., Chiapponi, C., Sani, G., Manfredi, G., Piras, F., Caltagirone, C., Spalletta, G., 2016. White matter microstructural characteristics in Bipolar I and Bipolar II Disorder: a diffusion tensor imaging study. J. Affect. Disord. 189, 176–183. https://doi.org/10.1016/j.jad.2015.09.035.

American Psychiatric Association (APA), 2022. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR). American Psychiatric Publishing, Arlington VA.

Benedetti, F., Yeh, P.H., Bellani, M., Radaelli, D., Nicoletti, M.A., Poletti, S., Falini, A., Dallaspezia, S., Colombo, C., Scotti, G., Smeraldi, E., Soares, J.C., Brambilla, P., 2011. Disruption of white matter integrity in bipolar depression as a possible structural marker of illness. Biol. Psychiatry 69, 309–317. https://doi.org/10.1016/j.biopsych.2010.07.028.

Bi, B., Che, D., Bai, Y., 2022. Neural network of bipolar disorder: toward integration of neuroimaging and neurocircuit-based treatment strategies. Transl. Psychiatry 12, 143. https://doi.org/10.1038/s41398-022-01917-x.

Bigot, M., Alonso, M., Houenou, J., Sarrazin, S., Dargél, A.A., Lledo, P.-M., Henry, C., 2020. An emotional-response model of bipolar disorders integrating recent findings on amygdala circuits. Neurosci. Biobehav. Rev. 118, 358–366. https://doi.org/10.1016/j.neubiorev.2020.07.037.

Blumberg, H.P., Stern, E., Martinez, D., Ricketts, S., de Asis, J., White, T., Epstein, J., McBride, P.A., Eidelberg, D., Kocsis, J.H., Silbersweig, D.A., 2000. Increased anterior cingulate and caudate activity in bipolar mania. Biol. Psychiatry 48, 1045–1052. https://doi.org/10.1016/s0006-3223(00)00962-8.

Bond, D.J., Ha, T.H., Lang, D.J., Su, W., Torres, I.J., Honer, W.G., Lam, R.W., Yatham, L. N., 2014. Body mass index-related regional gray and white matter volume reductions in first-episode mania patients. Biol. Psychiatry 76, 138–145. https://doi.org/10.1016/j.biopsych.2013.08.030.

Bora, E., 2025. A meta-analysis of data-driven cognitive subgroups in bipolar disorder. Eur. Neuropsychopharmacol. 90, 48–57. https://doi.org/10.1016/j.euroneuro.2024.10.008.

Bozikas, V., Tonia, T., Fokas, K., Karavatos, A., Kosmidis, M., 2006. Impaired emotion processing in remitted patients with bipolar disorder. J. Affect. Disord. 91, 53–56. https://doi.org/10.1016/j.jad.2005.11.013.

Brambilla, P., Harenski, K., Nicoletti, M.A., Mallinger, A.G., Frank, E., Kupfer, D.J., Keshavan, M.S., Soares, J.C., 2001. Anatomical MRI study of basal ganglia in bipolar disorder patients. Psychiatry Res. 106, 65–80. https://doi.org/10.1016/s0925-4927(01)00073-7.

Brambilla, P., Harenski, K., Nicoletti, M., Sassi, R.B., Mallinger, A.G., Frank, E., Kupfer, D.J., Keshavan, M.S., Soares, J.C., 2003. MRI investigation of temporal lobe structures in bipolar patients. J. Psychiatr. Res. 37, 287–295. https://doi.org/10.1016/S0022-3956(03)00024-4.

Brancati, G.E., Nunes, A., Scott, K., O'Donovan, C., Cervantes, P., Grof, P., Alda, M., 2023. Differential characteristics of bipolar I and II disorders: a retrospective, cross-sectional evaluation of clinical features, illness course, and response to treatment. Int. J. Bipolar Disord. 11, 25. https://doi.org/10.1186/s40345-023-00304-9.

Brosch, K., Stein, F., Schmitt, S., Pfarr, J.K., Ringwald, K.G., Thomas-Odenthal, F., Meller, T., Steinsträter, O., Waltemate, L., Lemke, H., Meinert, S., Winter, A., Breuer, F., Thiel, K., Grotegerd, D., Hahn, T., Jansen, A., Dannlowski, U., Krug, A., Nenadić, I., Kircher, T., 2022. Reduced hippocampal gray matter volume is a common feature of patients with major depression, bipolar disorder, and schizophrenia spectrum disorders. Mol. Psychiatry 27, 4234–4243. https://doi.org/10.1038/s41380-022-01687-4.

Canales-Rodríguez, E.J., Verdolini, N., Alonso-Lana, S., Torres, M.L., Panicalli, F., Argila-Plaza, I., Rodriguez-Cano, E., Montoro, I., Garcia-Ruiz, B., Jimenez, E., Varo, C., Lluch, A., Del Mar Bonnin, C., Maluf, S., Pujol, M., Guarner, N.J., Sarró, S., Vieta, E., Vilella, E., Salvador, R., Pomarol-Clotet, E., 2023. Widespread intra-axonal signal fraction abnormalities in bipolar disorder from multicompartment diffusion MRI: sensitivity to diagnosis, association with clinical features and pharmacologic treatment. Hum. Brain Mapp. 44, 4605–4622. https://doi.org/10.1002/hbm.26405.

Cao, B., Passos, I.C., Mwangi, B., Amaral-Silva, H., Tannous, J., Wu, M.-J., Zunta-Soares, G.B., Soares, J.C., 2017. Hippocampal subfield volumes in mood disorders. Mol. Psychiatry 22, 1352–1358. https://doi.org/10.1038/mp.2016.262.

Caseras, X., Lawrence, N.S., Murphy, K., Wise, R.G., Phillips, M.L., 2013. Ventral striatum activity in response to reward: differences between bipolar I and II disorders. AJP 170, 533–541. https://doi.org/10.1176/appi.ajp.2012.12020169.

Caseras, X., Murphy, K., Lawrence, N.S., Fuentes-Claramonte, P., Watts, J., Jones, D.K., Phillips, M.L., 2015. Emotion regulation deficits in euthymic bipolar I versus bipolar II disorder: a functional and diffusion-tensor imaging study. Bipolar Disord. 17, 461–470. https://doi.org/10.1111/bdi.12292.

Cattarinussi, G., Di Giorgio, A., Wolf, R.C., Balestrieri, M., Sambataro, F., 2019. Neural signatures of the risk for bipolar disorder: a meta-analysis of structural and functional neuroimaging studies. Bipolar Disord. 21, 215–227. https://doi.org/10.1111/bdi.12720.

Cattarinussi, G., Kubera, K.M., Hirjak, D., Wolf, R.C., Sambataro, F., 2022. Neural correlates of the risk for schizophrenia and bipolar disorder: a meta-analysis of structural and functional neuroimaging studies. Biol. Psychiatry 92, 375–384. https://doi.org/10.1016/j.biopsych.2022.02.960.

Cattarinussi, G., Di Giorgio, A., Moretti, F., Bondi, E., Sambataro, F., 2023a. Dynamic functional connectivity in schizophrenia and bipolar disorder: a review of the evidence and associations with psychopathological features. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 127, 110827. https://doi.org/10.1016/j.pnpbp.2023.110827.

Cattarinussi, G., Gugliotta, A.A., Sambataro, F., 2023b. The risk for schizophrenia-bipolar spectrum: does the apple fall close to the tree? A narrative review. Int. J. Environ. Res. Public Health 20, 6540. https://doi.org/10.3390/ijerph20156540.

Chance, S.A., Esiri, M.M., Crow, T.J., 2003. Ventricular enlargement in schizophrenia: a primary change in the temporal lobe? Schizophr. Res. 62, 123–131. https://doi.org/10.1016/s0920-9964(02)00344-4.

Charney, A.W., Ruderfer, D.M., Stahl, E.A., Moran, J.L., Chambert, K., Belliveau, R.A., Forty, L., Gordon-Smith, K., Di Florio, A., Lee, P.H., Bromet, E.J., Buckley, P.F., Escamilla, M.A., Fanous, A.H., Fochtmann, L.J., Lehrer, D.S., Malaspina, D., Marder, S.R., Morley, C.P., Nicolini, H., Perkins, D.O., Rakofsky, J.J., Rapaport, M. H., Medeiros, H., Sobell, J.L., Green, E.K., Backlund, L., Bergen, S.E., Juréus, A., Schalling, M., Lichtenstein, P., Roussos, P., Knowles, J.A., Jones, I., Jones, L.A., Hultman, C.M., Perlis, R.H., Purcell, S.M., McCarroll, S.A., Pato, C.N., Pato, M.T., Craddock, N., Landén, M., Smoller, J.W., Sklar, P., 2017. Evidence for genetic heterogeneity between clinical subtypes of bipolar disorder. Transl. Psychiatry 7, e993. https://doi.org/10.1038/tp.2016.242.

Chen, Y.L., Tu, P.C., Huang, T.H., Bai, Y.M., Su, T.P., Chen, M.H., Wu, Y.T., 2021a. Identifying subtypes of bipolar disorder based on clinical and neurobiological characteristics. Sci. Rep. 11, 17082. https://doi.org/10.1038/s41598-021-96645-5.

Chen, Y., Wang, X., Guan, L., Wang, Y., 2021b. Role of white matter hyperintensities and related risk factors in vascular cognitive impairment: a review. Biomolecules 11, 1102. https://doi.org/10.3390/biom11081102.

Chen, G., Wang, J., Gong, J., Qi, Z., Fu, S., Tang, G., Chen, P., Huang, L., Wang, Y., 2022. Functional and structural brain differences in bipolar disorder: a multimodal meta-analysis of neuroimaging studies. Psychol. Med. 52, 2861–2873. https://doi.org/10.1017/S0033291722002392.

Choi, K.W., Han, K.M., Kim, A., Kang, W., Kang, Y., Tae, W.S., Ham, B.J., 2022. Decreased cortical gyrification in patients with bipolar disorder. Psychol. Med. 52, 2232–2244. https://doi.org/10.1017/S0033291720004079.

Coombes, B.J., Markota, M., Mann, J.J., Colby, C., Stahl, E., Talati, A., Pathak, J., Weissman, M.M., McElroy, S.L., Frye, M.A., Biernacka, J.M., 2020. Dissecting clinical heterogeneity of bipolar disorder using multiple polygenic risk scores. Transl. Psychiatry 10, 314. https://doi.org/10.1038/s41398-020-00996-y.

Cui, Y., Dong, J., Yang, Y., Yu, H., Li, W., Liu, Y., Si, J., Xie, S., Sui, J., Lv, L., Jiang, T., 2020. White matter microstructural differences across major depressive disorder, bipolar disorder and schizophrenia: a tract-based spatial statistics study. J. Affect. Disord. 260, 281–286. https://doi.org/10.1016/j.jad.2019.09.029.

Cui, L., Li, H., Li, J.B., Zeng, H., Zhang, Y., Deng, W., Zhou, W., Cao, L., 2022. Altered cerebellar gray matter and cerebellar-cortex resting-state functional connectivity in patients with bipolar disorder I. J. Affect. Disord. 302, 50–57. https://doi.org/10.1016/j.jad.2022.01.073.

d'Arbeloff, T.C., Kim, M.J., Knodt, A.R., Radtke, S.R., Brigidi, B.D., Hariri, A.R., 2018. Microstructural integrity of a pathway connecting the prefrontal cortex and amygdala moderates the association between cognitive reappraisal and negative emotions. Emotion 18, 912–915. https://doi.org/10.1037/emo0000447.

De Prisco, M., Vieta, E., 2024. The never-ending problem: sample size matters. Eur. Neuropsychopharmacol. 79, 17–18. https://doi.org/10.1016/j.euroneuro.2023.10.002.

De Prisco, M., Oliva, V., Fico, G., Radua, J., Grande, I., Roberto, N., Anmella, G., Hidalgo-Mazzei, D., Fornaro, M., de Bartolomeis, A., Serretti, A., Vieta, E., Murru, A., 2023. Emotion dysregulation in bipolar disorder compared to other mental illnesses: a systematic review and meta-analysis. Psychol. Med. 53, 7484–7503. https://doi.org/10.1017/S003329172300243X.

Dell'Osso, B., Holtzman, J.N., Goffin, K.C., Portillo, N., Hooshmand, F., Miller, S., Dore, J., Wang, P.W., Hill, S.J., Ketter, T.A., 2015. American tertiary clinic-referred bipolar II disorder compared to bipolar I disorder: more severe in multiple ways, but less severe in a few other ways. J. Affect. Disord. 188, 257–262. https://doi.org/10.1016/j.jad.2015.09.001.

Dell'Osso, B., Dobrea, C., Cremaschi, L., Buoli, M., Miller, S., Ketter, T.A., Altamura, A.C., 2017. Italian bipolar II vs I patients have better individual functioning, in spite of overall similar illness severity. CNS Spectr. 22, 325–332. https://doi.org/10.1017/S1092852915000887.

Favre, P., Pauling, M., Stout, J., Hozer, F., Sarrazin, S., Abé, C., Alda, M., Alloza, C., Alonso-Lana, S., Andreassen, O.A., Baune, B.T., Benedetti, F., Busatto, G.F., Canales-Rodríguez, E.J., Caseras, X., Chaim-Avancini, T.M., Ching, C.R.K., Dannlowski, U., Deppe, M., Eyler, L.T., Fatjo-Vilas, M., Foley, S.F., Grotegerd, D., Hajek, T., Haukvik, U.K., Howells, F.M., Jahanshad, N., Kugel, H., Lagerberg, T.V., Lawrie, S. M., Linke, J.O., McIntosh, A., Melloni, E.M.T., Mitchell, P.B., Polosan, M., Pomarol-Clotet, E., Repple, J., Roberts, G., Roos, A., Rosa, P.G.P., Salvador, R., Sarró, S., Schofield, P.R., Serpa, M.H., Sim, K., Stein, D.J., Sussmann, J.E., Temmingh, H.S., Thompson, P.M., Verdolini, N., Vieta, E., Wessa, M., Whalley, H.C., Zanetti, M.V., Leboyer, M., Mangin, J.-F., Henry, C., Duchesnay, E., Houenou, J., ENIGMA Bipolar Disorder Working Group, 2019. Widespread white matter microstructural abnormalities in bipolar disorder: evidence from mega- and meta-analyses across 3033 individuals. Neuropsychopharmacol. 44, 2285–2293. https://doi.org/10.1038/s41386-019-0485-6.

Foley, S.F., Bracher-Smith, M., Tansey, K.E., Harrison, J.R., Parker, G.D., Caseras, X., 2018. Fractional anisotropy of the uncinate fasciculus and cingulum in bipolar disorder type I, type II, unaffected siblings and healthy controls. Br. J. Psychiatry 213, 548–554. https://doi.org/10.1192/bjp.2018.101.

Gerchen, M.F., Kirsch, P., 2017. Combining task-related activation and connectivity analysis of fMRI data reveals complex modulation of brain networks. Hum. Brain Mapp. 38, 5726–5739. https://doi.org/10.1002/hbm.23762.

Gitlin, M., Malhi, G.S., 2020. The existential crisis of bipolar II disorder. Int. J. Bipolar Disord. 8, 5. https://doi.org/10.1186/s40345-019-0175-7.

Goto, M., Abe, O., Hagiwara, A., Fujita, S., Kamagata, K., Hori, M., Aoki, S., Osada, T., Konishi, S., Masutani, Y., Sakamoto, H., Sakano, Y., Kyogoku, S., Daida, H., 2022. Advantages of using both voxel- and surface-based morphometry in cortical morphology analysis: a review of various applications. Magn. Reson. Med. Sci. 21, 41–57. https://doi.org/10.2463/mrms.rev.2021-0096.

Gutiérrez-Galve, L., Bruno, S., Wheeler-Kingshott, C.A.M., Summers, M., Cipolotti, L., Ron, M.A., 2012. IQ and the fronto-temporal cortex in bipolar disorder. J. Int. Neuropsychol. Soc. 18, 370–374. https://doi.org/10.1017/S1355617711001706.

Ha, T.H., Ha, K., Kim, J.H., Choi, J.E., 2009. Regional brain gray matter abnormalities in patients with bipolar II disorder: a comparison study with bipolar I patients and healthy controls. Neurosci. Lett. 456, 44–48. https://doi.org/10.1016/j.neulet.2009.03.077.

Ha, T.H., Her, J.Y., Kim, J.H., Chang, J.S., Cho, H.S., Ha, K., 2011. Similarities and differences of white matter connectivity and water diffusivity in bipolar I and II disorder. Neurosci. Lett. 505, 150–154. https://doi.org/10.1016/j.neulet.2011.10.009.

Hafeman, D.M., Chang, K.D., Garrett, A.S., Sanders, E.M., Phillips, M.L., 2012. Effects of medication on neuroimaging findings in bipolar disorder: an updated review. Bipolar Disord. 14, 375–410. https://doi.org/10.1111/j.1399-5618.2012.01023.x.

Haukvik, U.K., Gurholt, T.P., Nerland, S., Elvsåshagen, T., Akudjedu, T.N., Alda, M., Alnæs, D., Alonso-Lana, S., Bauer, J., Baune, B.T., Benedetti, F., Berk, M., Bettella, F., Bøen, E., Bonnín, C.M., Brambilla, P., Canales-Rodríguez, E.J., Cannon, D.M., Caseras, X., Dandash, O., Dannlowski, U., Delvecchio, G., Díaz-Zuluaga, A.M., Erp, T. G.M., Fatjó-Vilas, M., Foley, S.F., Förster, K., Fullerton, J.M., Goikolea, J.M., Grotegerd, D., Gruber, O., Haarman, B.C.M., Haatveit, B., Hajek, T., Hallahan, B., Harris, M., Hawkins, E.L., Howells, F.M., Hülsmann, C., Jahanshad, N., Jørgensen, K. N., Kircher, T., Krämer, B., Krug, A., Kuplicki, R., Lagerberg, T.V., Lancaster, T.M., Lenroot, R.K., Lonning, V., López-Jaramillo, C., Malt, U.F., McDonald, C., McIntosh, A.M., McPhilemy, G., Meer, D., Melle, I., Melloni, E.M.T., Mitchell, P.B., Nabulsi, L., Nenadić, I., Oertel, V., Oldani, L., Opel, N., Otaduy, M.C.G., Overs, B.J., Pineda-Zapata, J.A., Pomarol-Clotet, E., Radua, J., Rauer, L., Redlich, R., Repple, J., Rive, M.M., Roberts, G., Ruhe, H.G., Salminen, L.E., Salvador, R., Sarró, S., Savitz, J., Schene, A.H., Sim, K., Soeiro-de-Souza, M.G., Stäblein, M., Stein, D.J., Stein, F., Tamnes, C.K., Temmingh, H.S., Thomopoulos, S.I., Veltman, D.J., Vieta, E., Waltemate, L., Westlye, L.T., Whalley, H.C., Sämann, P.G., Thompson, P.M., Ching, C.R.K., Andreassen, O.A., Agartz, I., ENIGMA Bipolar Disorder Working Group, 2022. In vivo hippocampal subfield volumes in bipolar disorder—a mega-analysis from the Enhancing Neuro Imaging Genetics through Meta-Analysis Bipolar Disorder Working Group. Hum. Brain Mapp. 43, 385–398. https://doi.org/10.1002/hbm.25249.

Hauser, P., Matochik, J., Altshuler, L.L., Denicoff, K.D., Conrad, A., Li, X., Post, R.M., 2000. MRI-based measurements of temporal lobe and ventricular structures in patients with bipolar I and bipolar II disorders. J. Affect. Disord. 60, 25–32. https://doi.org/10.1016/S0165-0327(99)00154-8.

Hernandorena, C., Baldessarini, Tondo, L., Vàzquez, 2023. Status of type II vs. type I bipolar disorder: systematic review with meta-analyses. Harv. Rev. Psychiatry. https://doi.org/10.1097/HRP.0000000000000371.

Hernandorena, C., Dines, M., Miola, A., Nuñez, N.A., Tondo, L., Baldessarini, R.J., Vázquez, G.H., 2025. Clinical prescription of lithium, anticonvulsants antipsychotics, and antidepressants for major mood disorders. Int. J. Bipolar Disord. 13, 24. https://doi.org/10.1186/s40345-025-00381-y.

Hibar, D.P., Westlye, L.T., van Erp, T.G.M., Rasmussen, J., Leonardo, C.D., Faskowitz, J., Haukvik, U.K., Hartberg, C.B., Doan, N.T., Agartz, I., Dale, A.M., Gruber, O., Krämer, B., Trost, S., Liberg, B., Abé, C., Ekman, C.J., Ingvar, M., Landén, M., Fears, S.C., Freimer, N.B., Bearden, C.E., Costa Rica/Colombia Consortium for Genetic Investigation of Bipolar Endophenotypes, Sprooten, E., Glahn, D.C., Pearlson, G.D., Emsell, L., Kenney, J., Scanlon, C., McDonald, C., Cannon, D.M., Almeida, J., Versace, A., Caseras, X., Lawrence, N.S., Phillips, M.L., Dima, D., Delvecchio, G., Frangou, S., Satterthwaite, T.D., Wolf, D., Houenou, J., Henry, C., Malt, U.F., Bøen, E., Elvsåshagen, T., Young, A.H., Lloyd, A.J., Goodwin, G.M., Mackay, C.E., Bourne, C., Bilderbeck, A., Abramovic, L., Boks, M.P., van Haren, N.E. M., Ophoff, R.A., Kahn, R.S., Bauer, M., Pfennig, A., Alda, M., Hajek, T., Mwangi, B., Soares, J.C., Nickson, T., Dimitrova, R., Sussmann, J.E., Hagenaars, S., Whalley, H. C., McIntosh, A.M., Thompson, P.M., Andreassen, O.A., 2016. Subcortical volumetric abnormalities in bipolar disorder. Mol. Psychiatry 21, 1710–1716. https://doi.org/10.1038/mp.2015.227.

Hibar, D.P., Westlye, L.T., Doan, N.T., Jahanshad, N., Cheung, J.W., Ching, C.R.K., Versace, A., Bilderbeck, A.C., Uhlmann, A., Mwangi, B., Krämer, B., Overs, B., Hartberg, C.B., Abé, C., Dima, D., Grotegerd, D., Sprooten, E., Bøen, E., Jimenez, E., Howells, F.M., Delvecchio, G., Temmingh, H., Starke, J., Almeida, J.R.C., Goikolea, J.M., Houenou, J., Beard, L.M., Rauer, L., Abramovic, L., Bonnin, M., Ponteduro, M.F., Keil, M., Rive, M.M., Yao, N., Yalin, N., Najt, P., Rosa, P.G., Redlich, R., Trost, S., Hagenaars, S., Fears, S.C., Alonso-Lana, S., Van Erp, T.G.M., Nickson, T., Chaim-Avancini, T.M., Meier, T.B., Elvsåshagen, T., Haukvik, U.K., Lee, W.H., Schene, A.H., Lloyd, A.J., Young, A.H., Nugent, A., Dale, A.M., Pfennig, A., McIntosh, A.M., Lafer, B., Baune, B.T., Ekman, C.J., Zarate, C.A., Bearden, C.E., Henry, C., Simhandl, C., McDonald, C., Bourne, C., Stein, D.J., Wolf, D.H., Cannon, D.M., Glahn, D.C., Veltman, D.J., Pomarol-Clotet, E., Vieta, E., Canales-Rodriguez, E.J., Nery, F.G., Duran, F.L.S., Busatto, G.F., Roberts, G., Pearlson, G.D., Goodwin, G.M., Kugel, H., Whalley, H.C., Ruhe, H.G., Soares, J.C., Fullerton, J.M., Rybakowski, J.K., Savitz, J., Chaim, K.T., Fatjó-Vilas, M., Soeiro-de-Souza, M.G., Boks, M.P., Zanetti, M.V., Otaduy, M.C.G., Schaufelberger, M.S., Alda, M., Ingvar, M., Phillips, M.L., Kempton, M.J., Bauer, M., Landén, M., Lawrence, N.S., Van Haren, N.E.M., Horn, N.R., Freimer, N.B., Gruber, O., Schofield, P.R., Mitchell, P.B., Kahn, R.S., Lenroot, R., Machado-Vieira, R., Ophoff, R.A., Sarró, S., Frangou, S., Satterthwaite, T.D., Hajek, T., Dannlowski, U., Malt, U.F., Arolt, V., Gattaz, W.F., Drevets, W.C., Caseras, X., Agartz, I., Thompson, P.M., Andreassen, O.A., 2018. Cortical abnormalities in bipolar disorder: an MRI analysis of 6503 individuals from the ENIGMA bipolar disorder working group. Mol. Psychiatry 23, 932–942. https://doi.org/10.1038/mp.2017.73.

Horga, G., Bernacer, J., Dusi, N., Entis, J., Chu, K., Hazlett, E.A., Haznedar, M.M., Kemether, E., Byne, W., Buchsbaum, M.S., 2011. Correlations between ventricular enlargement and gray and white matter volumes of cortex, thalamus, striatum, and internal capsule in schizophrenia. Eur. Arch. Psychiatry Clin. Neurosci. 261, 467–476. https://doi.org/10.1007/s00406-011-0202-x.

Hunt, G.E., Malhi, G.S., Cleary, M., Lai, H.M., Sitharthan, T., 2016. Prevalence of comorbid bipolar and substance use disorders in clinical settings, 1990-2015: systematic review and meta-analysis. J. Affect. Disord. 206, 331–349. https://doi.org/10.1016/j.jad.2016.07.011.

Ilzarbe, L., Vieta, E., 2023. The elephant in the room: medication as confounder. Eur. Neuropsychopharmacol. 71, 6–8. https://doi.org/10.1016/j.euroneuro.2023.03.001.

Janiri, D., Sani, G., De Rossi, P., Piras, F., Banaj, N., Ciullo, V., Simonetti, A., Arciniegas, D.B., Spalletta, G., 2019. Hippocampal subfield volumes and childhood trauma in bipolar disorders. J. Affect. Disord. 253, 35–43. https://doi.org/10.1016/j.jad.2019.04.071.

Jin, K., Zhang, T., Shaw, M., Sachdev, P., Cherbuin, N., 2018. Relationship between sulcal characteristics and brain aging. Front. Aging Neurosci. 10, 339. https://doi.org/10.3389/fnagi.2018.00339.

Karanti, A., Kardell, M., Joas, E., Runeson, B., Pålsson, E., Landén, M., 2020. Characteristics of bipolar I and II disorder: a study of 8766 individuals. Bipolar Disord. 22, 392–400. https://doi.org/10.1111/bdi.12867.

Kieseppä, T., Mäntylä, R., Luoma, K., Rikandi, E., Jylhä, P., Isometsä, E., 2022. White matter hyperintensities after five-year follow-up and a cross-sectional FA decrease in bipolar I and major depressive patients. Neuropsychobiology 81, 39–50. https://doi.org/10.1159/000516234.

Kim, Jooyeon, Cho, H., Kim, Jinha, Kim, A., Kang, Y., Kang, W., Choi, K.W., Ham, B.-J., Han, K.-M., Tae, W.-S., 2020. Changes in cortical thickness and volume of cerebellar subregions in patients with bipolar disorders. J. Affect. Disord. 271, 74–80. https://doi.org/10.1016/j.jad.2020.03.087.

Koshiyama, D., Fukunaga, M., Okada, N., Morita, K., Nemoto, K., Usui, K., Yamamori, H., Yasuda, Y., Fujimoto, M., Kudo, N., Azechi, H., Watanabe, Y., Hashimoto, N., Narita, H., Kusumi, I., Ohi, K., Shimada, T., Kataoka, Y., Yamamoto, M., Ozaki, N., Okada, G., Okamoto, Y., Harada, K., Matsuo, K., Yamasue, H., Abe, O., Hashimoto, R., Takahashi, T., Hori, T., Nakataki, M., Onitsuka, T., Holleran, L., Jahanshad, N., van Erp, T.G.M., Turner, J., Donohoe, G., Thompson, P.M., Kasai, K., Hashimoto, R., COCORO, 2020. White matter microstructural alterations across four major psychiatric disorders: mega-analysis study in 2937 individuals. Mol. Psychiatry 25, 883–895. https://doi.org/10.1038/s41380-019-0553-7.

Kotoula, V., Evans, J.W., Punturieri, C.E., Zarate Jr., C.A., 2023. Review: the use of functional magnetic resonance imaging (fMRI) in clinical trials and experimental research studies for depression. Front. Neuroimaging. 2, 1110258. https://doi.org/10.3389/fnimg.2023.1110258.

Kringelbach, M.L., 2005. The human orbitofrontal cortex: linking reward to hedonic experience. Nat. Rev. Neurosci. 6, 691–702. https://doi.org/10.1038/nrn1747.

Libero, L.E., DeRamus, T.P., Deshpande, H.D., Kana, R.K., 2014. Surface-based morphometry of the cortical architecture of autism spectrum disorders: volume, thickness, area, and gyrification. Neuropsychologia 62, 1–10. https://doi.org/10.1016/j.neuropsychologia.2014.07.001.

Lin, F., Weng, S., Xie, B., Wu, G., Lei, H., 2011. Abnormal frontal cortex white matter connections in bipolar disorder: a DTI tractography study. J. Affect. Disord. 131, 299–306. https://doi.org/10.1016/j.jad.2010.12.018.

Liu, J.-X., Chen, Y.-S., Hsieh, J.-C., Su, T.-P., Yeh, T.-C., Chen, L.-F., 2010. Differences in white matter abnormalities between bipolar I and II disorders. J. Affect. Disord. 127, 309–315. https://doi.org/10.1016/j.jad.2010.05.026.

Liu, W., Jiang, X., Deng, Z., Jia, L., Sun, Q., Kong, L., Wu, F., Tang, Y., 2022. Altered dynamic amplitude of low-frequency fluctuation between bipolar type I and type II in the depressive state. NeuroImage Clin. 36, 103184. https://doi.org/10.1016/j.nicl.2022.103184.

Lupo, M., Olivito, G., Siciliano, L., Masciullo, M., Molinari, M., Cercignani, M., Bozzali, M., Leggio, M., 2018. Evidence of cerebellar involvement in the onset of a manic state. Front. Neurol. 9, 774. https://doi.org/10.3389/fneur.2018.00774.

Lyoo, I.K., Sung, Y.H., Dager, S.R., Friedman, S.D., Lee, J.-Y., Kim, S.J., Kim, N., Dunner, D.L., Renshaw, P.F., 2006. Regional cerebral cortical thinning in bipolar disorder. Bipolar Disord. 8, 65–74. https://doi.org/10.1111/j.1399-5618.2006.00284.x.

Malhi, G.S., Outhred, T., Irwin, L., 2019. Bipolar II disorder is a myth. Can. J. Psychiatr., 070674371984734 https://doi.org/10.1177/0706743719847341.

Maller, J.J., Thaveenthiran, P., Thomson, R.H., McQueen, S., Fitzgerald, P.B., 2014. Volumetric, cortical thickness and white matter integrity alterations in bipolar disorder type I and II. J. Affect. Disord. 169, 118–127. https://doi.org/10.1016/j.jad.2014.08.016.

Maller, J.J., Anderson, R., Thomson, R.H., Rosenfeld, J.V., Daskalakis, Z.J., Fitzgerald, P.B., 2015. Occipital bending (Yakovlevian torque) in bipolar depression. Psychiatry Res. Neuroimaging 231, 8–14. https://doi.org/10.1016/j.pscychresns.2014.11.008.

Matsumoto, J., Fukunaga, M., Miura, K., Nemoto, K., Okada, N., Hashimoto, N., Morita, K., Koshiyama, D., Ohi, K., Takahashi, T., Koeda, M., Yamamori, H., Fujimoto, M., Yasuda, Y., Ito, S., Yamazaki, R., Hasegawa, N., Narita, H., Yokoyama, S., Mishima, R., Miyata, J., Kobayashi, Y., Sasabayashi, D., Harada, K., Yamamoto, M., Hirano, Y., Itahashi, T., Nakataki, M., Hashimoto, R.I., Tha, K.K., Koike, S., Matsubara, T., Okada, G., Yoshimura, R., Abe, O., van Erp, T.G.M., Turner, J.A., Jahanshad, N., Thompson, P.M., Onitsuka, T., Watanabe, Y., Matsuo, K., Yamasue, H., Okamoto, Y., Suzuki, M., Ozaki, N., Kasai, K., Hashimoto, R., 2023. Cerebral cortical structural alteration patterns across four major psychiatric disorders in 5549 individuals. Mol. Psychiatry 28, 4915–4923. https://doi.org/10.1038/s41380-023-02224-7.

McDonald, C., 2015. Brain structural effects of psychopharmacological treatment in bipolar disorder. Curr. Neuropharmacol. 13, 445–457. https://doi.org/10.2174/1570159x13666150403231654.

McWhinney, S.R., Abé, C., Alda, M., Benedetti, F., Bøen, E., Del Mar Bonnin, C., Borgers, T., Brosch, K., Canales-Rodríguez, E.J., Cannon, D.M., Dannlowski, U., Díaz-Zuluaga, A.M., Elvsåshagen, T., Eyler, L.T., Fullerton, J.M., Goikolea, J.M., Goltermann, J., Grotegerd, D., Haarman, B.C.M., Hahn, T., Howells, F.M., Ingvar, M., Kircher, T.T.J., Krug, A., Kuplicki, R.T., Landén, M., Lemke, H., Liberg, B., Lopez-Jaramillo, C., Malt, U.F., Martyn, F.M., Mazza, E., McDonald, C., McPhilemy, G., Meier, S., Meinert, S., Meller, T., Melloni, E.M.T., Mitchell, P.B., Nabulsi, L., Nenadic, I., Opel, N., Ophoff, R.A., Overs, B.J., Pfarr, J.K., Pineda-Zapata, J.A., Pomarol-Clotet, E., Raduà, J., Repple, J., Richter, M., Ringwald, K.G., Roberts, G., Salvador, R., Savitz, J., Schmitt, S., Schofield, P.R., Sim, K., Stein, D.J., Stein, F., Temmingh, H.S., Thiel, K., van Haren, N.E.M., Gestel, H.V., Vargas, C., Vieta, E., Vreeker, A., Waltemate, L., Yatham, L.N., Ching, C.R.K., Andreassen, O., Thompson, P.M., Hajek, T., ENIGMA Bipolar Disorders Working Group, 2021. Association between body mass index and subcortical brain volumes in bipolar disorders-ENIGMA study in 2735 individuals. Mol. Psychiatry 26, 6806–6819. https://doi.org/10.1038/s41380-021-01098-x.

McWhinney, S.R., Abé, C., Alda, M., Benedetti, F., Bøen, E., Del Mar Bonnin, C., Borgers, T., Brosch, K., Canales-Rodríguez, E.J., Cannon, D.M., Dannlowski, U., Diaz-Zuluaga, A.M., Dietze, L., Elvsåshagen, T., Eyler, L.T., Fullerton, J.M., Goikolea, J.M., Goltermann, J., Grotegerd, D., Haarman, B.C.M., Hahn, T., Howells, F.M., Ingvar, M., Kircher, T.T.J., Krug, A., Kuplicki, R.T., Landén, M., Lemke, H., Liberg, B., Lopez-Jaramillo, C., Malt, U.F., Martyn, F.M., Mazza, E., McDonald, C., McPhilemy, G., Meier, S., Meinert, S., Meller, T., Melloni, E.M.T., Mitchell, P.B., Nabulsi, L., Nenadic, I., Opel, N., Ophoff, R.A., Overs, B.J., Pfarr, J.K., Pineda-Zapata, J.A., Pomarol-Clotet, E., Raduà, J., Repple, J., Richter, M., Ringwald, K.G., Roberts, G., Ross, A., Salvador, R., Savitz, J., Schmitt, S., Schofield, P.R., Sim, K., Stein, D.J., Stein, F., Temmingh, H.S., Thiel, K., Thomopoulos, S.I., van Haren, N.E.M., Van Gestel, H., Vargas, C., Vieta, E., Vreeker, A., Waltemate, L., Yatham, L.N., Ching, C.R.K., Andreassen, O.A., Thompson, P.M., Hajek, T., ENIGMA Bipolar Disorders Working Group, 2022. Diagnosis of bipolar disorders and body mass index predict clustering based on similarities in cortical thickness-ENIGMA study in 2436 individuals. Bipolar Disord. 24, 509–520. https://doi.org/10.1111/bdi.13172.

Meinert, S., Nowack, N., Grotegerd, D., Repple, J., Winter, N.R., Abheiden, I., Enneking, V., Lemke, H., Waltemate, L., Stein, F., Brosch, K., Schmitt, S., Meller, T., Pfarr, J.K., Ringwald, K., Steinsträter, O., Gruber, M., Nenadić, I., Krug, A., Leehr, E. J., Hahn, T., Thiel, K., Dohm, K., Winter, A., Opel, N., Schubotz, R.I., Kircher, T., Dannlowski, U., 2022. Association of brain white matter microstructure with cognitive performance in major depressive disorder and healthy controls: a diffusion-tensor imaging study. Mol. Psychiatry 27, 1103–1110. https://doi.org/10.1038/s41380-021-01330-8.

Mesbah, R., Koenders, M.A., Van Der Wee, N.J.A., Giltay, E.J., Van Hemert, A.M., De Leeuw, M., 2023. Association between the fronto-limbic network and cognitive and emotional functioning in individuals with bipolar disorder: a systematic review and meta-analysis. JAMA Psychiatry 80, 432. https://doi.org/10.1001/jamapsychiatry.2023.0131.

Miola, A., Cattarinussi, G., Antiga, G., Caiolo, S., Solmi, M., Sambataro, F., 2022a. Difficulties in emotion regulation in bipolar disorder: a systematic review and meta-analysis. J. Affect. Disord. 302, 352–360. https://doi.org/10.1016/j.jad.2022.01.102.

Miola, A., Cattarinussi, G., Loré, M.L., Ghiotto, N., Collantoni, E., Sambataro, F., 2022b. Brain gyrification in bipolar disorder: a systematic review of neuroimaging studies. Brain Imaging Behav. 16, 2768–2784. https://doi.org/10.1007/s11682-022-00713-x.

Miola, A., Trevisan, N., Merola, A., Comini, F.F., Olivo, D., Minerva, M., Valeggia, S., Toffanin, T., Favaro, A., Manara, R., Sambataro, F., 2022c. Gray matter volume covariance networks are associated with altered emotional processing in bipolar disorder: a source-based morphometry study. Brain Imaging Behav. 16, 738–747. https://doi.org/10.1007/s11682-021-00541-5.

Miola, A., De Filippis, E., Veldic, M., Ho, A.M., Winham, S.J., Mendoza, M., Romo-Nava, F., Nunez, N.A., Gardea Resendez, M., Prieto, M.L., McElroy, S.L., Biernacka, J.M., Frye, M.A., Cuellar-Barboza, A.B., 2022d. The genetics of bipolar disorder with obesity and type 2 diabetes. J. Affect. Disord. 313, 222–231. https://doi.org/10.1016/j.jad.2022.06.084.

Miola, A., Fountoulakis, K.N., Baldessarini, R.J., Veldic, M., Solmi, M., Rasgon, N., Ozerdem, A., Perugi, G., Frye, M.A., Preti, A., 2023a. Prevalence and outcomes of rapid cycling bipolar disorder: mixed method systematic meta-review. J. Psychiatr. Res. 164, 404–415. https://doi.org/10.1016/j.jpsychires.2023.06.021.

Miola, A., Tondo, L., Pinna, M., Contu, M., Baldessarini, R.J., 2023b. Characteristics of rapid cycling in 1261 bipolar disorder patients. Int. J. Bipolar Disord. 11, 21. https://doi.org/10.1186/s40345-023-00300-z.

Miola, A., Trevisan, N., Salvucci, M., Minerva, M., Valeggia, S., Manara, R., Sambataro, F., 2023c. Network dysfunction of sadness facial expression processing and morphometry in euthymic bipolar disorder. Eur. Arch. Psychiatry Clin. Neurosci. 274, 525–536. https://doi.org/10.1007/s00406-023-01649-z.

Mørch-Johnsen, L., Jørgensen, K.N., Barth, C., Nerland, S., Bringslid, I.K., Wortinger, L. A., Andreou, D., Melle, I., Andreassen, O.A., Agartz, I., 2023. Thalamic nuclei volumes in schizophrenia and bipolar spectrum disorders - associations with diagnosis and clinical characteristics. Schizophr. Res. 256, 26–35. https://doi.org/10.1016/j.schres.2023.04.008.

Müller, V.I., Cieslik, E.C., Laird, A.R., Fox, P.T., Radua, J., Mataix-Cols, D., Tench, C.R., Yarkoni, T., Nichols, T.E., Turkeltaub, P.E., Wager, T.D., Eickhoff, S.B., 2018. Ten simple rules for neuroimaging meta-analysis. Neurosci. Biobehav. Rev. 84, 151–161. https://doi.org/10.1016/j.neubiorev.2017.11.012.

Nusslock, R., Glazer, J., Ng, T.H., Titone, M.K., Alloy, L.B., 2019. Reward hypersensitivity in bipolar spectrum disorders: from mechanisms to markers to treatment. In: Gruber, J. (Ed.), The Oxford Handbook of Positive Emotion and Psychopathology. Oxford University Press, pp. 161–183. https://doi.org/10.1093/oxfordhb/9780190653200.013.11.

O'Connell, K.S., Koromina, M., van der Veen, T., Boltz, T., David, F.S., Yang, J.M.K., Bipolar Disorder Working Group of the Psychiatric Genomics Consortium, et al., 2025. Genomics yields biological and phenotypic insights into bipolar disorder. Nature. https://doi.org/10.1038/s41586-024-08468-9.

Oliva, V., Fico, G., De Prisco, M., Gonda, X., Rosa, A.R., Vieta, E., 2024. Bipolar disorders: an update on critical aspects. Lancet Reg. Health Eur. 48, 101135. https://doi.org/10.1016/j.lanepe.2024.101135.

Olivito, G., Lupo, M., Siciliano, L., Gragnani, A., Saettoni, M., Pancheri, C., Panfili, M., Pignatelli, F., Delle Chiaie, R., Leggio, M., 2022a. Theory of mind profile and cerebellar alterations in remitted bipolar disorder 1 and 2: a comparison study. Front. Behav. Neurosci. 16, 971244. https://doi.org/10.3389/fnbeh.2022.971244.

Olivito, G., Lupo, M., Gragnani, A., Saettoni, M., Siciliano, L., Pancheri, C., Panfili, M., Cercignani, M., Bozzali, M., Chiaie, R.D., Leggio, M., 2022b. Aberrant cerebello-cerebral connectivity in remitted bipolar patients 1 and 2: new insight into

understanding the cerebellar role in mania and hypomania. Cerebellum 21, 647–656. https://doi.org/10.1007/s12311-021-01317-9.
Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D., Shamseer, L., Tetzlaff, J.M., Akl, E.A., Brennan, S.E., Chou, R., Glanville, J., Grimshaw, J.M., Hróbjartsson, A., Lalu, M.M., Li, T., Loder, E.W., Mayo-Wilson, E., McDonald, S., McGuinness, L.A., Stewart, L.A., Thomas, J., Tricco, A.C., Welch, V.A., Whiting, P., Moher, D., 2021. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 372, n71. https://doi.org/10.1136/bmj.n71.
Parker, G.B., Graham, R.K., Hadzi-Pavlovic, D., 2016. Are the bipolar disorders best modelled categorically or dimensionally? Acta Psychiatr. Scand. 134, 104–110. https://doi.org/10.1111/acps.12567.
Parker, G., Spoelma, M.J., Tavella, G., Alda, M., Hajek, T., Dunner, D.L., O'Donovan, C., Rybakowski, J.K., Goldberg, J.F., Bayes, A., Sharma, V., Boyce, P., Manicavasagar, V., 2020. The bipolar disorders: a case for their categorically distinct status based on symptom profiles. J. Affect. Disord. 277, 225–231. https://doi.org/10.1016/j.jad.2020.08.014.
Patel, A., Biso, G.M.N.R., Fowler, J.B., 2023. Neuroanatomy. In: Temporal Lobe. StatPearls Publishing, Treasure Island (FL).
Pedersen, W.S., Dean, D.C., Adluru, N., Gresham, L.K., Lee, S.D., Kelly, M.P., Mumford, J. A., Davidson, R.J., Schaefer, S.M., 2022. Individual variation in white matter microstructure is related to better recovery from negative stimuli. Emotion 22, 244–257. https://doi.org/10.1037/emo0000996.
Preti, A., Vrublevska, J., Veroniki, A.A., Huedo-Medina, T.B., Fountoulakis, K.N., 2016. Prevalence, impact and treatment of generalised anxiety disorder in bipolar disorder: a systematic review and meta-analysis. Evid. Based Ment. Health 19, 73–81. https://doi.org/10.1136/eb-2016-102412.
Preti, A., Vrublevska, J., Veroniki, A.A., Huedo-Medina, T.B., Kyriazis, O., Fountoulakis, K.N., 2018. Prevalence and treatment of panic disorder in bipolar disorder: systematic review and meta-analysis. Evid. Based Ment. Health 21, 53–60. https://doi.org/10.1136/eb-2017-102858.
Richards, A.L., Cardno, A., Harold, G., Craddock, N.J., Di Florio, A., Jones, L., Gordon-Smith, K., Jones, I., Sellers, R., Walters, J.T.R., Holmans, P.A., Owen, M.J., O'Donovan, M.C., 2022. Genetic liabilities differentiating bipolar disorder, schizophrenia, and major depressive disorder, and phenotypic heterogeneity in bipolar disorder. JAMA Psychiatr. 79, 1032–1039. https://doi.org/10.1001/jamapsychiatry.2022.2594.
Sani, G., Simonetti, A., Janiri, D., Banaj, N., Ambrosi, E., De Rossi, P., Ciullo, V., Arciniegas, D.B., Piras, F., Spalletta, G., 2018. Association between duration of lithium exposure and hippocampus/amygdala volumes in type I bipolar disorder. J. Affect. Disord. 232, 341–348. https://doi.org/10.1016/j.jad.2018.02.042.
Savitz, J., Nugent, A.C., Bogers, W., Liu, A., Sills, R., Luckenbaugh, D.A., Bain, E.E., Price, J.L., Zarate, C., Manji, H.K., Cannon, D.M., Marrett, S., Charney, D.S., Drevets, W.C., 2010. Amygdala volume in depressed patients with bipolar disorder assessed using high resolution 3T MRI: the impact of medication. Neuroimage 49, 2966–2976. https://doi.org/10.1016/j.neuroimage.2009.11.025.
Schiweck, C., Arteaga-Henriquez, G., Aichholzer, M., Edwin Thanarajah, S., Vargas-Cáceres, S., Matura, S., Grimm, O., Haavik, J., Kittel-Schneider, S., Ramos-Quiroga, J.A., Faraone, S.V., Reif, A., 2021. Comorbidity of ADHD and adult bipolar disorder: a systematic review and meta-analysis. Neurosci. Biobehav. Rev. 124, 100–123. https://doi.org/10.1016/j.neubiorev.2021.01.017.
Schumer, M.C., Chase, H.W., Rozovsky, R., Eickhoff, S.B., Phillips, M.L., 2023. Prefrontal, parietal, and limbic condition-dependent differences in bipolar disorder: a large-scale meta-analysis of functional neuroimaging studies. Mol. Psychiatry 28, 2826–2838. https://doi.org/10.1038/s41380-023-01974-8.
Silva, T., Nunes, C., Ribeiro, A., Santana, I., Cerejeira, J., 2024. White matter hyperintensities in bipolar disorder: systematic review and meta-analysis. Front. Psychiatry 15, 1343463. https://doi.org/10.3389/fpsyt.2024.1343463.
Smitha, K.A., Akhil Raja, K., Arun, K.M., Rajesh, P.G., Thomas, B., Kapilamoorthy, T.R., Kesavadas, C., 2017. Resting state fMRI: a review on methods in resting state connectivity analysis and resting state networks. Neuroradiol. J. 30, 305–317. https://doi.org/10.1177/1971400917697342.
Squarcina, L., Bellani, M., Rossetti, M.G., Perlini, C., Delvecchio, G., Dusi, N., Barillari, M., Ruggeri, M., Altamura, C.A., Bertoldo, A., Brambilla, P., 2017. Similar white matter changes in schizophrenia and bipolar disorder: a tract-based spatial statistics study. PLoS One 12, e0178089. https://doi.org/10.1371/journal.pone.0178089.
Strakowski, S.M., DelBello, M.P., Adler, C., Cecil, K.M., Sax, K.W., 2000. Neuroimaging in bipolar disorder: MRI in bipolar disorder. Bipolar Disord. 2, 148–164. https://doi.org/10.1034/j.1399-5618.2000.020302.x.
Sussmann, J.E., Lymer, G.K., McKirdy, J., Moorhead, T.W., Muñoz Maniega, S., Job, D., Hall, J., Bastin, M.E., Johnstone, E.C., Lawrie, S.M., McIntosh, A.M., 2009. White matter abnormalities in bipolar disorder and schizophrenia detected using diffusion tensor magnetic resonance imaging. Bipolar Disord. 11, 11–18. https://doi.org/10.1111/j.1399-5618.2008.00646.x.
Svancer, P., Spaniel, F., 2021. Brain ventricular volume changes in schizophrenia. A narrative review. Neurosci. Lett. 759, 136065. https://doi.org/10.1016/j.neulet.2021.136065.
Tai, H., Kandeel, N., Menon, M., Ibrahim, A., Choo, B., Santana, R., Jolayemi, A., 2024. Role of the cerebellum in bipolar disorder: a systematic literature review. Cureus 16, e56044. https://doi.org/10.7759/cureus.56044.
Thiel, K., Meinert, S., Winter, A., Lemke, H., Waltemate, L., Breuer, F., Gruber, M., Leenings, R., Wüste, L., Rüb, K., Pfarr, J.K., Stein, F., Brosch, K., Meller, T., Ringwald, K.G., Nenadić, I., Krug, A., Repple, J., Opel, N., Koch, K., Leehr, E.J., Bauer, J., Grotegerd, D., Hahn, T., Kircher, T., Dannlowski, U., 2023. Reduced fractional anisotropy in bipolar disorder *v.* major depressive disorder independent of current symptoms. Psychol. Med. 53, 4592–4602. https://doi.org/10.1017/S0033291722001490.
Thiel, K., Lemke, H., Winter, A., Flinkenflügel, K., Waltemate, L., Bonnekoh, L., Grotegerd, D., Dohm, K., Hahn, T., Förster, K., Kanske, P., Repple, J., Opel, N., Redlich, R., David, F., Forstner, A.J., Stein, F., Brosch, K., Thomas-Odenthal, F., Usemann, P., Teutenberg, L., Straube, B., Alexander, N., Jamalabadi, H., Jansen, A., Witt, S.H., Andlauer, T.F.M., Pfennig, A., Bauer, M., Nenadić, I., Kircher, T., Meinert, S., Dannlowski, U., 2024. White and gray matter alterations in bipolar I and bipolar II disorder subtypes compared with healthy controls - exploring associations with disease course and polygenic risk. Neuropsychopharmacology 49, 814–823. https://doi.org/10.1038/s41386-024-01812-7.
Tighe, S.K., Reading, S.A., Rivkin, P., Caffo, B., Schweizer, B., Pearlson, G., Potash, J.B., Depaulo, J.R., Bassett, S.S., 2012. Total white matter hyperintensity volume in bipolar disorder patients and their healthy relatives. Bipolar Disord. 14, 888–893. https://doi.org/10.1111/bdi.12019.
Tondo, L., Miola, A., Pinna, M., Contu, M., Baldessarini, R.J., 2022. Differences between bipolar disorder types 1 and 2 support the DSM two-syndrome concept. Int. J. Bipolar Disord. 10, 21. https://doi.org/10.1186/s40345-022-00268-2.
Vancampfort, D., Mitchell, A.J., De Hert, M., Sienaert, P., Probst, M., Buys, R., Stubbs, B., 2015. Prevalence and predictors of type 2 diabetes mellitus in people with bipolar disorder: a systematic review and meta-analysis. J. Clin. Psychiatry 76, 1490–1499. https://doi.org/10.4088/JCP.14r09635.
Versace, A., Almeida, J.R., Hassel, S., Walsh, N.D., Novelli, M., Klein, C.R., Kupfer, D.J., Phillips, M.L., 2008. Elevated left and reduced right orbitomedial prefrontal fractional anisotropy in adults with bipolar disorder revealed by tract-based spatial statistics. Arch. Gen. Psychiatry 65, 1041–1052. https://doi.org/10.1001/archpsyc.65.9.1041.
Videtta, G., Squarcina, L., Rossetti, M.G., Brambilla, P., Delvecchio, G., Bellani, M., 2023. White matter modifications of corpus callosum in bipolar disorder: a DTI tractography review. J. Affect. Disord. 338, 220–227. https://doi.org/10.1016/j.jad.2023.06.012.
Vieta, E., 2019. Bipolar II disorder: frequent, valid, and reliable. Can. J. Psychiatr. 64, 541–543. https://doi.org/10.1177/0706743719855040.
Vieta, E., De Prisco, M., 2024. Cross-sectional studies: is pressing the pause button worth it in research? Eur. Neuropsychopharmacol. 85, 32–33. https://doi.org/10.1016/j.euroneuro.2024.06.005.
Vieta, E., Berk, M., Schulze, T.G., Carvalho, A.F., Suppes, T., Calabrese, J.R., Gao, K., Miskowiak, K.W., Grande, I., 2018. Bipolar disorders. Nat. Rev. Dis. Primers 4, 18008. https://doi.org/10.1038/nrdp.2018.8.
Wang, Y., Gao, Y., Tang, S., Lu, L., Zhang, L., Bu, X., Li, H., Hu, Xiaoxiao, Hu, Xinyu, Jiang, P., Jia, Z., Gong, Q., Sweeney, J.A., Huang, X., 2020. Large-scale network dysfunction in the acute state compared to the remitted state of bipolar disorder: a meta-analysis of resting-state functional connectivity. EBioMedicine 54, 102742. https://doi.org/10.1016/j.ebiom.2020.102742.
Wei, S.-Y., Tseng, H.-H., Chang, H.H., Chang, W.H., Yang, Y.K., Chen, P.S., 2022. Associations of leptin and corticostriatal connectivity in bipolar disorder. Sci. Rep. 12, 21898. https://doi.org/10.1038/s41598-022-26233-8.
Wise, T., Radua, J., Via, E., Cardoner, N., Abe, O., Adams, T.M., Amico, F., Cheng, Y., Cole, J.H., de Azevedo Marques Périco, C., Dickstein, D.P., Farrow, T.F.D., Frodl, T., Wagner, G., Gotlib, I.H., Gruber, O., Ham, B.J., Job, D.E., Kempton, M.J., Kim, M.J., Koolschijn, P.C.M.P., Malhi, G.S., Mataix-Cols, D., McIntosh, A.M., Nugent, A.C., O'Brien, J.T., Pezzoli, S., Phillips, M.L., Sachdev, P.S., Salvadore, G., Selvaraj, S., Stanfield, A.C., Thomas, A.J., van Tol, M.J., van der Wee, N.J.A., Veltman, D.J., Young, A.H., Fu, C.H., Cleare, A.J., Arnone, D., 2017. Common and distinct patterns of grey-matter volume alteration in major depression and bipolar disorder: evidence from voxel-based meta-analysis. Mol. Psychiatry 22, 1455–1463. https://doi.org/10.1038/mp.2016.72.
Woo, Y., Kang, W., Kang, Y., Kim, A., Han, K.-M., Tae, W.-S., Ham, B.-J., 2021. Cortical thickness and surface area abnormalities in bipolar I and II disorders. Psychiatry Investig. 18, 850–863. https://doi.org/10.30773/pi.2021.0074.
Yang, C., Li, L., Hu, X., Luo, Q., Kuang, W., Lui, S., Huang, X., Dai, J., He, M., Kemp, G.J., Sweeney, J.A., Gong, Q., 2019. Psychoradiologic abnormalities of white matter in patients with bipolar disorder: diffusion tensor imaging studies using tract-based spatial statistics. J. Psychiatry Neurosci. 44, 32–44. https://doi.org/10.1503/jpn.170221.
Yang, T., Lam, R.W., Huang, J., Su, Y., Liu, J., Yang, X., Yang, L., Zhu, N., Zhao, G., Mao, R., Zhou, R., Xia, W., Liu, H., Wang, Z., Chen, J., Fang, Y., 2021. Exploring the effects of temperament on gray matter volume of frontal cortex in patients with mood disorders. Neuropsychiatr. Dis. Treat. 17, 183–193. https://doi.org/10.2147/NDT.S287351.
Zilles, K., Armstrong, E., Schleicher, A., Kretschmann, H.J., 1988. The human pattern of gyrification in the cerebral cortex. Anat. Embryol. (Berl.) 179, 173–179. https://doi.org/10.1007/BF00304699.
Zou, Q.H., Zhu, C.Z., Yang, Y., Zuo, X.N., Long, X.Y., Cao, Q.J., Wang, Y.F., Zang, Y.F., 2008. An improved approach to detection of amplitude of low-frequency fluctuation (ALFF) for resting-state fMRI: fractional ALFF. J. Neurosci. Methods 172, 137–141. https://doi.org/10.1016/j.jneumeth.2008.04.012.