Psychological Medicine

cambridge.org/psm

Functional and structural brain differences in bipolar disorder: a multimodal meta-analysis of neuroimaging studies

Guanmao Chen[1,2,*], Junjing Wang[3,*], Jiaying Gong[2,4,*], Zhangzhang Qi[1,2], Siying Fu[1,2], Guixian Tang[1,2], Pan Chen[1,2], Li Huang[1,2] and Ying Wang[1,2]

[1]Medical Imaging Center, First Affiliated Hospital of Jinan University, Guangzhou, 510630, China; [2]Institute of Molecular and Functional Imaging, Jinan University, Guangzhou, 510630, China; [3]Department of Applied Psychology, Guangdong University of Foreign Studies, Guangzhou, 510006, China and [4]Department of Radiology, the Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, 510655, China

Review Article

*Guanmao Chen, Junjing Wang and Jiaying Gong contributed equally to this work.

Cite this article: 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. *Psychological Medicine* **52**, 2861–2873. https://doi.org/10.1017/S0033291722002392

Received: 24 October 2021
Revised: 26 May 2022
Accepted: 12 July 2022
First published online: 12 September 2022

Key words:
bipolar disorder; meta-analysis; multimodal; resting-state functional imaging; voxel-based morphometry

Author for correspondence:
Ying Wang, E-mail: johneil@vip.sina.com

Abstract

Background. Numerous studies of resting-state functional imaging and voxel-based morphometry (VBM) have revealed differences in specific brain regions of patients with bipolar disorder (BD), but the results have been inconsistent.

Methods. A whole-brain voxel-wise meta-analysis was conducted on resting-state functional imaging and VBM studies that compared differences between patients with BD and healthy controls using Seed-based *d* Mapping with Permutation of Subject Images software.

Results. A systematic literature search identified 51 functional imaging studies (1842 BD and 2190 controls) and 83 VBM studies (2790 BD and 3690 controls). Overall, patients with BD displayed increased resting-state functional activity in the left middle frontal gyrus, right inferior frontal gyrus (IFG) extending to the right insula, right superior frontal gyrus and bilateral striatum, as well as decreased resting-state functional activity in the left middle temporal gyrus extending to the left superior temporal gyrus and post-central gyrus, left cerebellum, and bilateral precuneus. The meta-analysis of VBM showed that patients with BD displayed decreased VBM in the right IFG extending to the right insula, temporal pole and superior temporal gyrus, left superior temporal gyrus extending to the left insula, temporal pole, and IFG, anterior cingulate cortex, left superior frontal gyrus (medial prefrontal cortex), left thalamus, and right fusiform gyrus.

Conclusions. The multimodal meta-analyses suggested that BD showed similar patterns of aberrant brain activity and structure in the insula extending to the temporal cortex, fronto-striatal-thalamic, and default-mode network regions, which provide useful insights for understanding the underlying pathophysiology of BD.

Introduction

Bipolar disorder (BD) is a recurrent, chronic and severe disease, which is characterized by episodes of depression and mania/hypomania that cause serious harm to patients, families and society (Merikangas et al., 2007). It is one of the main causes of disability among young people, leading to cognitive impairment and increased mortality, especially deaths by suicide. Although numerous structural and functional neuroimaging studies have revealed differences in specific brain regions and connections in patients with BD, the neurobiology of BD using neuroimaging is not fully understood.

Over the past decade, blood oxygenation level-dependent (BOLD) functional magnetic resonance imaging (fMRI) has developed rapidly and become a promising tool to investigate the different brain activity regions in patients with BD, greatly improving our understanding of the neurobiological mechanisms of BD (Chen, Suckling, Lennox, Ooi, & Bullmore, 2011; Gong et al., 2020; Hajek, Alda, Hajek, & Ivanoff, 2013). A task-based meta-fMRI study of neurocognitive performance reported that BD patients showed under-activation in the right inferior frontal gyrus (IFG) and hyper-activation in the left superior temporal gyrus (Hajek et al., 2013). Another cognitive and emotional task-based meta-analysis (Chen et al., 2011) demonstrated IFG differences during both cognitive and emotional processing, and limbic hyper-activation during emotional processing. However, the results of task-based fMRI studies may be highly heterogeneous due to the differences in experimental design and the tasks (Bennett & Miller, 2010). Resting-state functional imaging provides a non-invasive and task-free approach that eliminates some of the performance-related confounders and provides a reliable method to measure baseline brain activities (Biswal, Yetkin, Haughton, & Hyde, 1995). Resting-state functional imaging methods include multiple imaging modalities, such as single-photon emission computed tomography (SPECT), positron emission tomography

© The Author(s), 2022. Published by Cambridge University Press

(PET), arterial spin labeling (ASL), amplitude of low-frequency fluctuation (ALFF), fractional ALFF, and regional homogeneity (ReHo). In SPECT and PET, radiotracers are used to measure cerebral blood flow (CBF) or brain metabolism. The BOLD signal does not directly measure the neuronal activity. In contrast, the BOLD effect is sensitive to the changes in CBF, the cerebral metabolic rate of oxygen, and cerebral blood volume, which are collectively referred to as activated hemodynamic responses (Buxton, Uludağ, Dubowitz, & Liu, 2004; Liu, Zhuo, & Yu, 2016). ASL technology can simultaneously identify BOLD signal and CBF (Buxton et al., 2004). The advantage of ASL is that it is a completely non-invasive MRI method that uses magnetically labeled water as an endogenous tracer to measure CBF. ALFF/fALFF quantifies the intensity of low-frequency oscillations in spontaneous neural activity. ReHo reflects the similarity of spontaneous neural activity between adjacent brain tissues. Previous resting-state functional imaging studies and related meta-analyses (Gong et al., 2020; Toma, MacIntosh, Swardfager, & Goldstein, 2018; Vargas et al., 2013) found different spontaneous brain activities in BD. However, these results are inconsistent. On one hand, different directions of activity of the same brain regions were reported between studies. For example, (Brooks, Hoblyn, & Ketter, 2010) and (Brooks, Hoblyn, Woodard, Rosen, & Ketter, 2009) reported significant hypometabolism in the prefrontal gyrus in BD while (Liu et al., 2012b) and (Xu et al., 2014a) reported increased activities in the prefrontal gyrus in BD. (Bøen, Hjørnevik, & Hummelen, 2019) reported hypometabolism in the striatum in BD. (Zhang et al., 2017) and (Zhang et al., 2020b) reported increased activities in the striatum in BD. On the other hand, different brain regions were reported in different studies, such as different functional activities in the prefrontal gyrus (Brooks et al., 2009, 2010; Liu et al., 2012a; Xu et al., 2014), insula (Liu et al., 2012a), striatum (Bøen et al., 2019; Zhang et al., 2017; Zhang et al., 2020b), temporal gyrus (Brooks et al., 2009, 2010; Liu et al., 2012a; Qiu et al., 2018), amygdala (Brooks et al., 2009), parahippocampal gyrus (Brooks et al., 2009, 2010), precuneus (Brooks et al., 2010; Qiu et al., 2018), parietal gyrus (Liu et al., 2012b; Qiu et al., 2018), and lingual gyrus (Qiu et al., 2018) in BD. These differences may be related to gender, age range, different subtypes and BD states (i.e. manic, depressed, mixed or euthymic), drug status, and methodology. There is no meta-analysis on the spontaneous neural activity in resting-state in BD by combining various functional imaging techniques.

In addition to functional alterations, morphological differences in the brains of patients with BD were found in previous structural MRI studies. Voxel-based morphometrics (VBM) is the most widely used analytical method to investigate structural differences in BD. VBM is an automatic whole-brain method that can calculate the local volume of gray matter in an unbiased manner. Existing VBM studies of BD have reported inconsistent results showing reduced gray matter volume (GMV) in the prefrontal gyrus (Almeida et al., 2009; Alonso-Lana et al., 2016; Altamura et al., 2018; Ambrosi et al., 2013; Brown et al., 2011; Cai et al., 2015; Eker et al., 2014), temporal gyrus (Ambrosi et al., 2013; Brown et al., 2011; Chen, Wen, Malhi, Ivanovski, & Sachdev, 2007; Cui et al., 2011), cingulate gyrus(Cai et al., 2015; Oertel-Knochel et al., 2014), parietal gyrus (Cui et al., 2011; Li et al., 2011), precuneus/ cuneus (Oertel-Knochel et al., 2014), hippocampus(Hajek et al., 2012, 2014), increased GMV in the putamen (Chen et al., 2012; Cui et al., 2011; Frangou, 2012), and no difference in GMV (Bruno, Barker, Cercignani, Symms, & Ron, 2004; Kandilarova, Stoyanov, Sirakov, & Maes, 2019). Consequently, several VBM meta-analyses have been conducted to summarize the existing evidence to map brain regions associated with BD (Ellison-Wright & Bullmore, 2010; Ganzola & Duchesne, 2017; Houenou et al., 2011; Lu et al., 2019; McCarthy, Liang, Spadoni, Kelsoe, & Simmons, 2014; Selvaraj et al., 2012; Wang et al., 2018a). However, the results of these meta-analyses were inconsistent, which may be attributed to certain factors. First, these meta-analyses included small number of trials, and most of these included fewer than 15 experiments (Ellison-Wright & Bullmore, 2010; Ganzola & Duchesne, 2017; Houenou et al., 2011; McCarthy et al., 2014; Selvaraj et al., 2012). In addition, the inclusion and exclusion criteria of the study were not strict, due to which unrelated variables such as repeated inclusion of subjects, periodicity of disease, and primary diagnosis of disease influenced the results (Ellison-Wright & Bullmore, 2010; Ganzola & Duchesne, 2017; Houenou et al., 2011; Lu et al., 2019; McCarthy et al., 2014; Selvaraj et al., 2012; Wang et al., 2018a). Recently, Lu et al., investigated gray matter deficits in the temporal and prefrontal cortex, and increased GMV in the putamen, cingulate cortex, and precuneus (46 studies with 56 experiments including 1720 subjects)(Lu et al., 2019). Given that several VBM studies(Chen et al., 2020b; Lee et al., 2020; Li et al., 2020; Sun et al., 2020; Vai et al., 2020) have been conducted in recent years, it is necessary to update the meta-analyses to expand and /or modify the findings of previous studies. In addition, most studies adopted a separate structural MRI to investigate BD. More efforts should be made to focus on the overlap of structural and functional imaging modalities to explore the neuropathological mechanisms in BD.

Hence, we aimed to conduct a whole-brain voxel-wise meta-analysis to explore the most robust findings across numerous published resting-state functional imaging studies and VBM studies, and to investigate whether there is a structural basis for functional impairment in some specific brain regions in BD. We hypothesized that BD patients have local convergence of GM decrease and increase and/or decrease in brain function compared with the control group. Moreover, we speculated that spontaneous functional activity and structural differences in BD are mainly located in the frontal and temporal gyri. The findings of this meta-analysis could facilitate further original research and help to further understand the pathophysiological mechanism of BD.

Methods

Data sources, study selection, and quality assessment

We followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses international guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009) (registration number is: CRD42021270700). A comprehensive search of studies published was conducted between January 1990 and January 2021 in the PubMed, Embase, Web of Science, SinoMed, Chinese National Knowledge Infrastructure, and WanFang databases using the following keywords: ('bipolar disorder' OR 'bipolar disorders' OR 'disorder, bipolar' OR 'psychosis, manic-depressive' OR 'psychosis, manic depressive' OR 'manic-depressive psychosis' OR 'manic depressive psychosis' OR 'affective psychosis, bipolar' OR 'bipolar affective psychosis' OR 'psychoses, bipolar affective' OR 'psychosis, bipolar affective' OR 'psychoses, manic-depressive' OR 'manic-depressive psychoses' OR 'psychoses, manic depressive'

https://doi.org/10.1017/S0033291722002392 Published online by Cambridge University Press

OR 'mania' OR 'manias' OR 'manic state' OR 'manic states' OR 'state, manic' OR 'states, manic' OR 'depression, bipolar' OR 'bipolar depression' OR 'manic disorder' OR 'disorder, manic' OR 'manic disorders') AND ('neuroimag*' OR 'functional magnetic resonance imaging' OR 'fMRI' OR 'cerebral blood flow' OR 'CBF' OR 'positron emission tomography' OR 'PET' OR 'single photon emission computed tomography' OR 'SPECT' OR 'arterial spin labeling' OR 'ASL' OR 'amplitude of low-frequency fluctuation' OR 'ALFF' OR 'fractional ALFF' OR 'fALFF' OR 'regional homogeneity' OR 'ReHo' OR 'resting-state' OR 'Voxel-based morphometry' OR 'VBM' OR 'morphometry'). In addition, we also checked the reference list of included studies and related review articles to identify other relevant studies.

Studies that satisfied the following conditions were included in the meta-analysis. (1) Subjects were aged from 18 to 60 years old. (2) They compared resting-state functional imaging or GMV between BD and healthy controls (HCs). (3) Three-dimensional coordinates [Talairach or Montreal Neurological Institute (MNI)] were reported for whole-brain resting-state functional imaging or GMV analysis. (4) The study was published as an original article (not as an abstract or a letter) in a peer-reviewed English or Chinese language journal. (5) Significant results were reported using thresholds for significance corrected for multiple comparisons or uncorrected with spatial extent thresholds. And (6) When the original manuscripts' details were not reported, it could be available by making a reasonable request to the corresponding author.

Studies were excluded if (1) patients with BD with comorbid neurological diseases; (2) the data overlapped with those of another included publication; (3) the data were unavailable (e.g. missing neuroanatomical coordinates) even after the authors were contacted by telephone or email; (4) a region-of-interest approach was used.

We used a 10-point checklist involved in the previous meta-analysis of neuroimaging studies to assess the quality of each study selected for this meta-analysis (online Supplementary Table S1 in Supplementary materials) (Chen et al., 2015; Shepherd, Matheson, Laurens, Carr, & Green, 2012). Literature search, study evaluation, and selection were independently performed by three investigators (G.J.Y., Q.S.J., and C.P.). Any discrepancies were resolved by a third investigator (W.Y.) for a final decision. The current study was conducted with reference to the Meta-analysis of Observational Studies in Epidemiology guidelines for the meta-analyses of observational studies(Stroup et al., 2000).

Data analysis

Voxel-wise meta-analysis for functional differences

A meta-analysis of functional (i.e. Reho, ALFF, fALFF, and CBF) differences between BD and HCs was conducted using the Seed-based *d* Mapping with Permutation of Subject Images (SDM-PSI version 6.21) software package in a standard process (www.sdmproject.com). The SDM-PSI is a voxel-based meta-analysis software using peak coordinates and their *t* values as reported from the original studies, to impute multiple effect-size maps (Hedges' effect size) of contrast results (increased and decreased activations) for each study. Thereafter, the maps are combined in a standard random-effects model based on sample size, intra-study variability and inter-study heterogeneity (Radua et al., 2012b), and multiple imputations are pooled using Rubin's rules(Albajes-Eizagirre, Solanes, Vieta, & Radua, 2019b). The familywise error rate (FWER) of the results is calculated using a subject-based permutation test. SDM-PSI uses MetaNSUE (Albajes-Eizagirre, Solanes, & Radua, 2019a) to estimate the maximum likely effect size within the lower and upper limits of possible effect sizes for each study separately, and then adds realistic noise (Albajes-Eizagirre et al., 2019b). We performed the analysis as described in the SDM tutorial and related publications, using MRIcron software (www.mricro.com/mricron/) to visualize the SDM maps.

Briefly, whole-brain meta-analyses were performed to assess functional differences between BD and HCs. Residual heterogeneity (I^2 statistic) of included studies was examined to assess the robustness of results ($I^2 > 50\%$ commonly indicates serious heterogeneity). Funnel plots were created to visually examine if findings had been driven by a small subset of studies or by studies with small sample sizes. We reported results using an uncorrected $p < 0.005$ threshold with a cluster extent = 10 voxels, since it was found to optimally balance sensitivity and specificity(Radua et al., 2012a, 2012b). Complementary analyses were conducted using FWER-corrected $p < 0.05$ with the threshold-free cluster enhancement approach and 5000 permutations(Smith & Nichols, 2009).

In addition, for the thresholded meta-analytic results, meta-regression analysis was performed to assess the effects of illness duration, age, gender and FWHM in data-preprocessing, which could potentially influence the analytic results. In this step, we also used an uncorrected $p < 0.005$ threshold with a cluster extent = 10 voxels.

To further examine the specific functional differences between BD and HCs, subgroup meta-analyses were conducted for indices of Reho and ALFF, as well as in the unmedicated and depressed subgroups. There were not sufficient studies [minimum of 10 studies recommended for SDM meta-analyses (Carlisi et al., 2017; Radua & Mataix-Cols, 2009) of fALFF, PET, ASL, and patients in a manic state to conduct subgroup analyses.

Voxel-wise meta-analysis for structural differences

Similar to the meta-analyses for functional differences, we also conducted a meta-analysis for structural (i.e. VBM) differences between BD and HCs. However, meta-regression analysis was not conducted due to the limited number of studies (<10 studies).

Functional and structural overlap

To reveal both the functional and structural differences in BD, we investigated the overlap of functional and structural differences via overlapping thresholded meta-analytic results-maps.

Results

Included studies and sample characteristics

A flow diagram of the identification and exclusion of studies was presented in Fig. 1. For the functional meta-analysis, 57 experiments from 51 studies comprising 1842 patients with BD and 2190 HCs were selected. No significant differences were observed between patients with BD and HCs with respect to age [95% confidence interval (CI) = −3.444 to 2.755, $t = -0.220$, $p = 0.826$] or gender distribution (based on totals across all studies) ($\chi^2 = 1.431$, $p = 0.232$).

Further, for the specific analysis, 13 studies from 13 publications comprising 441 patients with BD and 462 HCs were selected for the unmedicated functional meta-analysis. 20 studies from 20

https://doi.org/10.1017/S0033291722002392 Published online by Cambridge University Press

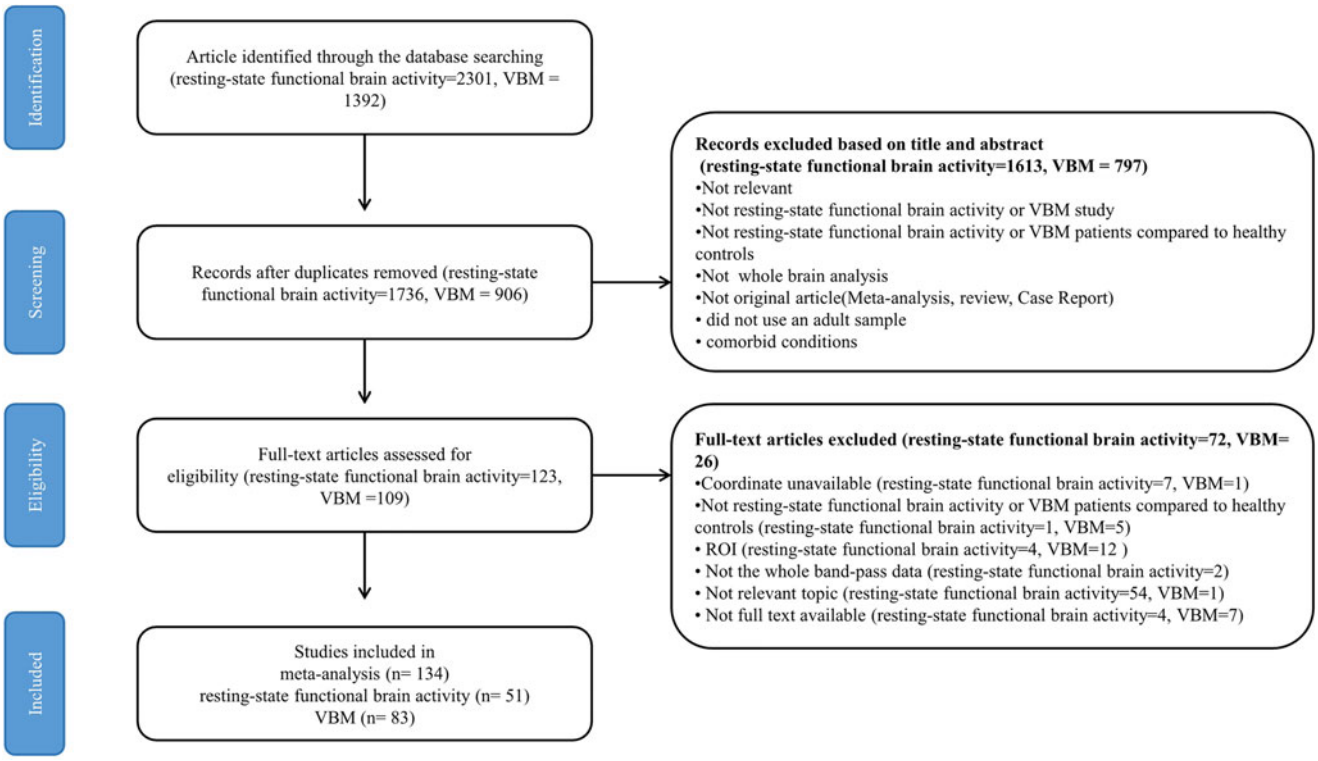


Fig. 1. Flow diagram for the identification and exclusion of resting-state functional imaging and VBM studies of patients with BD. Abbreviations: VBM, voxel-based morphometry; ROI, region of interest; BD, bipolar disorder.

publications comprising 644 patients with BD and 890 HCs were selected for the depressed functional meta-analysis. 22 studies from 20 publications comprising 751 patients with BD and 1188 HCs were selected for the Reho meta-analysis. 20 studies from 20 publications comprising 722 patients with BD and 969 HCs were selected for the ALFF analysis.

For the structural meta-analysis, 92 experiments from 83 studies comprising 2790 patients with BD and 3690 HCs were selected. No significant difference was observed between patients with BD and HCs with respect to age [95% confidence interval (CI) = −0.466 to 3.685, $t = 1.530$, $p = 0.128$] or gender distribution (based on totals across all studies) ($\chi^2 = 0.791$, $p = 0.374$).

The demographic, clinical, imaging characteristics, and quality scores of the included studies in this meta-analysis were well described in online Supplementary Tables S2 and S3 in Supplementary materials.

Functional meta-analysis

In the functional meta-analysis, patients with BD displayed increased resting-state functional activity in the left middle frontal gyrus, right IFG (extending to the right insula), right superior frontal gyrus and bilateral striatum, as well as decreased resting-state functional activity in the left middle temporal gyrus (extending to the left superior temporal gyrus and post-central gyrus), left cerebellum, and bilateral precuneus (Fig. 2a and Table 1). In addition to the right striatum, the inter-study heterogeneity for each significant peak was low ($I^2 < 50\%$). Funnel plots suggested that the results were not driven by small or noisy studies, and the potential publication bias was not statistically significant ($p > 0.05$). In the complementary analyses, persistent increased resting-state functional activity in the left middle frontal gyrus and decreased resting-state functional activity in the left middle temporal gyrus (extending to the left superior temporal gyrus and post-central gyrus) were observed in BD after FWE correction (online Supplementary Fig. S1a and Table S4). Additionally, we did not detect any significant result for the meta-regression analyses.

In the subgroup analyses, patients with BD in a depressed state displayed increased resting-state functional activity in the left IFG, and decreased resting-state functional activity in the left post-central gyrus (online Supplementary Fig. S2a and Table S5). The inter-group heterogeneity for the left IFG was high ($I^2 > 50\%$), while for the left post-central gyrus was low ($I^2 < 50\%$). Funnel plots suggested that the results were not driven by small or noisy studies, and the potential publication bias was not statistically significant ($p > 0.05$).

In the unmedicated functional meta-analysis, BD patients without medication showed increased resting-state functional activity in the bilateral superior frontal gyrus and right post-central gyrus (online Supplementary Fig. S2b and Table S6). The inter-study heterogeneity for each significant peak was low ($I^2 < 50\%$). Funnel plots suggested that the results were not driven by small or noisy studies, and the potential publication bias was not statistically significant ($p > 0.05$).

In the Reho meta-analysis, patients with BD displayed increased Reho in the left middle frontal gyrus, and decreased Reho in the left middle temporal gyrus (online Supplementary Fig. S3a and Table S7). The inter-study heterogeneity for each significant peak was low ($I^2 < 50\%$). Funnel plots suggested that the results were not driven by small or noisy studies, and the potential publication bias was not statistically significant ($p > 0.05$).

https://doi.org/10.1017/S0033291722002392 Published online by Cambridge University Press

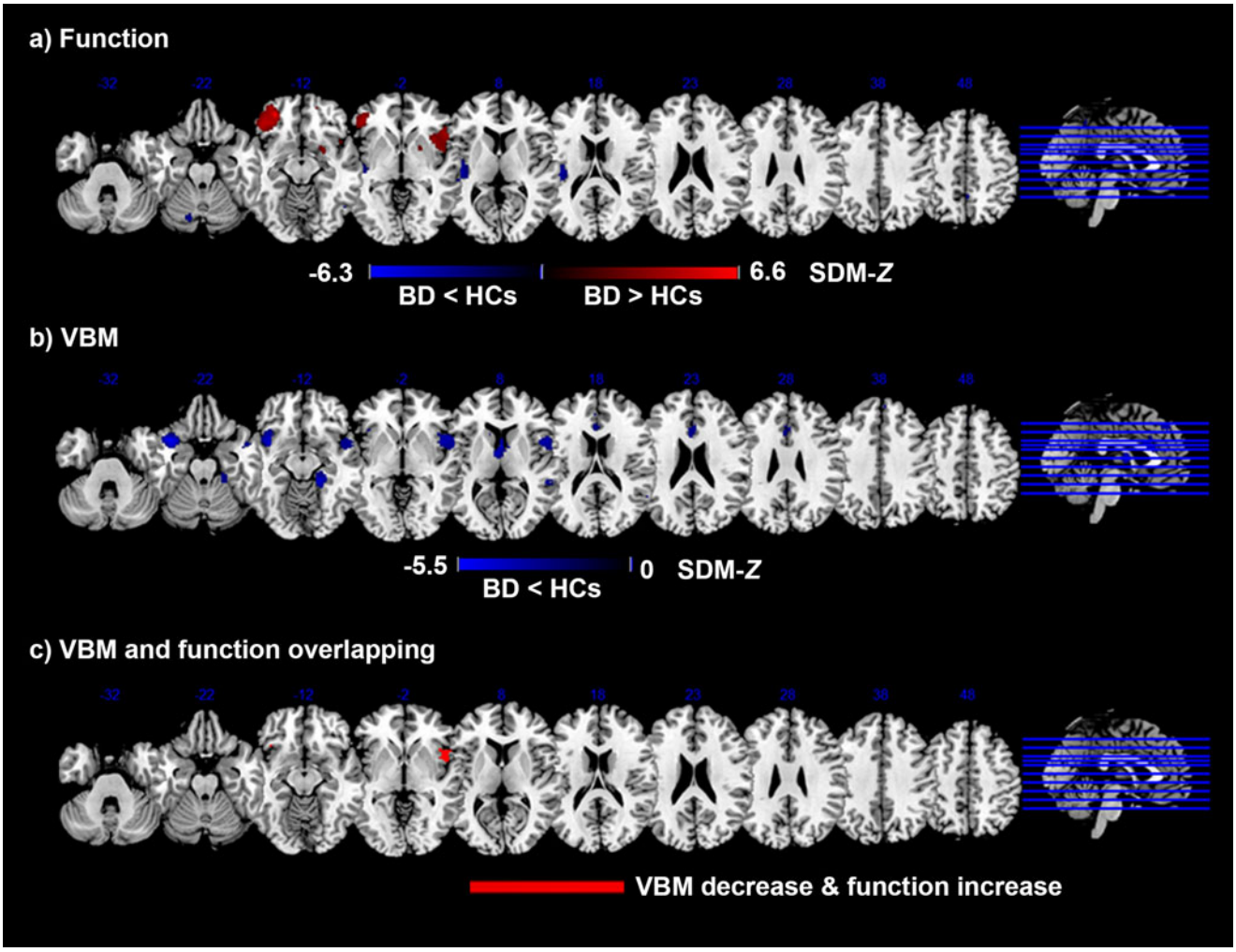


Fig. 2. Meta-analyses results regarding (a) resting-state functional activity difference between BD and HCs, (b) GMV difference between BD and HCs, (c) conjunction of resting-state functional activity differences and GMV differences. Areas with decreased value are displayed in blue, and areas with increased value are displayed in red. The color bar indicates the maximum and minimum SDM-*Z* values. Abbreviations: BD, bipolar disorder; HCs, healthy controls; GMV, gray matter volume; SDM, signed differential mapping.

In the ALFF meta-analysis, patients with BD displayed increased ALFF in the right insula, bilateral IFG, bilateral striatum, bilateral caudate nucleus, right inferior temporal gyrus, as well as decreased ALFF in the left cerebellum (online Supplementary Fig. S3b and Table S8). The inter-study heterogeneity for each significant peak was low ($I^2 < 50\%$). Funnel plots suggested that the results were not driven by small or noisy studies, and the potential publication bias was not statistically significant ($p > 0.05$).

Structural meta-analysis

In the VBM meta-analysis, we found that patients with BD displayed decreased VBM in the right IFG (extending to the right insula, temporal pole and superior temporal gyrus), left superior temporal gyrus (extending to the left insula, temporal pole, and IFG), anterior cingulate cortex (ACC), left superior frontal gyrus (medial prefrontal cortex, mPFC), left thalamus, and right fusiform gyrus (Fig. 2b and Table 2). In addition to the left ACC inter-study heterogeneity for each significant peak was low ($I^2 < 50\%$). Funnel plots suggested that the results were not driven by small or noisy studies, and the potential publication bias was not statistically significant ($p > 0.05$). In the complementary analyses, decreased VBM persisted in the left temporal pole after FWER correction (online Supplementary Fig. S1b and Table S9).

Overlap of functional and VBM differences

After overlapping the functional and VBM differences based on the above meta-analyses, patients with BD showed increased resting-state functional activity and decreased VBM in the right insula (Fig. 2c).

Discussion

To the best of our knowledge, this is the first multimodal neuroimaging meta-analysis including a large number of whole brain studies investigating spontaneous functional activity (51 studies with 57 experiments including 4032 subjects) as well as studies investigating structural gray matter (83 studies with 92 experiments including 6480 subjects) to more consistently localize the neural substrates of BD. In the resting-state functional imaging

https://doi.org/10.1017/S0033291722002392 Published online by Cambridge University Press

https://doi.org/10.1017/S0033291722002392 Published online by Cambridge University Press

Table 1. Meta-analyses results regarding the functional difference between BD and HCs

Local maximum				Cluster			
region	Peak MNI coordinate (*x*, *y*, *z*)	SDM-*Z* value	*p* value	No. of voxels	Breakdown (No. of voxels)	I^2	Egger's test (*p* value)
BD > HCs							
Left middle frontal gyrus, orbital part, BA 11	−26, 46, −16	5.437	$<10^{-10}$	1377	Left inferior frontal gyrus, orbital part, BAs 11, 38, 45, 46, 47 (655) Left middle frontal gyrus, orbital part, BAs 11, 46, 47 (350) Left inferior frontal gyrus, triangular part, BAs 45, 47 (68)	28.471	0.803
Right inferior frontal gyrus, triangular part, BA 45	50, 24, 0	4.637	1.788×10^{-6}	559	Right insula, BAs 38, 47, 48 (304) Right inferior frontal gyrus, triangular part, BAs 45, 47 (80) Right inferior frontal gyrus, opercular part, BAs 45, 48 (45) Right temporal pole, superior temporal gyrus (11)	14.624	0.755
Right striatum	18, 10, −8	3.387	3.536×10^{-4}	106	Right striatum (45) Right lenticular nucleus, putamen, BA 48 (12)	50.261	0.862
Right superior frontal gyrus, dorsolateral, BA 8	18, 22, 52	3.235	6.083×10^{-4}	32	Right superior frontal gyrus, dorsolateral, BA 8 (16) Right middle frontal gyrus, BA 8 (15)	1.505	0.796
Left striatum	−20, 12, −2	3.042	1.176×10^{-3}	14		12.292	0.857
BD < HCs							
Left middle temporal gyrus, BA 22	−58, −16, 0	−6.211	$<10^{-10}$	2243	Left superior temporal gyrus, BAs 22, 42, 48 (796) Left postcentral gyrus, BAs 22, 48 (140) Left heschl gyurs, BA 48 (118) Left middle temporal gyrus, BAs 21, 22, 48 (176) Let supramarginal gyrus, BAs 42, 48 (113) Left insula, BA 48 (33)	25.163	0.649
Right precuneus, BA 5	8, −48, 54	−3.752	8.779×10^{-5}	144	Right precuneus (96) Left precuneus (45)	42.511	0.484
Left cerebellum, hemispheric lobule VI, BA 18	−14, −72, −18	−4.065	2.402×10^{-5}	75		24.510	0.925

Abbreviations: BD, bipolar disorder; HCs, healthy controls; MNI, Montreal Neurological Institute; SDM, signed differential mapping; BA, Brodmann area.

https://doi.org/10.1017/S0033291722002392 Published online by Cambridge University Press

Table 2. Meta-analyses results regarding VBM difference between BD and HCs

Local maximum				Cluster			
region	Peak MNI coordinate (*x*, *y*, *z*)	SDM-*Z* value	*p* value	No. of voxels	Breakdown (No. of voxels)	I^2	Egger's test (*p* value)
BD < HCs							
Right inferior frontal gyrus, opercular part, BA 48	52, 10, 4	−4.134	1.782×10^{-5}	785	Right insula (169) Right temporal pole, superior temporal gyrus, BAs 21, 38, 48 (207) Right inferior frontal gyrus, opercular part, BAs 44, 48 (101) Right temporal pole, middle temporal gyurs, BA 21 (17) Right superior temporal gyrus, BAs 21, 38, 48 (29) Right middle temporal gyrus, BA 21 (11)	45.390	0.412
Left temporal pole, superior temporal gyrus, BA 38	−38, 10, −22	−5.504	$<10^{-10}$	528	Left temporal pole, superior temporal gyrus (243) Left insula, BAs 38, 47, 48 (124) Left inferior frontal gyrus, orbital part, BAs 38, 47 (46)	<10-4	0.929
Right fusiform gyrus	20, −36, −16	−4.476	3.815×10^{-6}	282	Right fusiform gyrus, BAs 30, 37 (87) Right parahippocampal gyrus, BA 30 (52) Right cerebellum, hemispheric lobule IV/V, BA 30 (29)	39.465	0.374
Left thalamus	−4, −6, 10	−4.162	1.579×10^{-5}	229		31.062	0.701
Left anterior cingulate / paracingulate gyri, BA 24	−2, 22, 22	−3.294	4.937×10^{-4}	159	Left anterior cingulate / paracingulate gyri (93) Right anterior cingulate / paracingulate gyri, BA 24 (30) Left median network, cingulum (12)	58.811	0.976
Right superior temporal gyrus, BA 42	60, −36, 12	−3.326	3.312×10^{-4}	85	Right superior temporal gyrus, BAs 22, 42 (47) Right middle temporal gyrus, BAs 21, 22 (28)	8.491	0.563
Left superior frontal gyrus, medial, BA 9	−2, 40, 44	−3.741	9.179×10^{-5}	55		9.094	0.709

Abbreviations: BD, bipolar disorder; HCs, healthy controls; VBM, voxel-based morphometry; MNI, Montreal Neurological Institute; SDM, signed differential mapping; BA, Brodmann area.

meta-analysis, BD showed increased spontaneous functional activity in the bilateral ventrolateral prefrontal cortex (extending to the insula) and bilateral striatum, and decreased functional activity in the left middle temporal gyrus (extending to the superior temporal gyrus), precuneus and cerebellum. In the VBM meta-analysis, BD showed decreased GMV in the bilateral ACC, mPFC, bilateral temporal pole (extending to the insula, superior temporal gyrus, and IFG), left thalamus, and right fusiform gyrus. Furthermore, there were large overlapping functional and anatomical changes in the right insula in BD. These functional and structural alterations provide important insights into the pathophysiological substrate of BD.

The insula is a cortical structure with extensive connections to the frontal cortex, ACC, parietal lobe, temporal lobe, amygdala, dorsal thalamus and other limbic areas(Augustine, 1996), which is implicated in various cognitive, affective, and regulatory functions, including interoceptive awareness, emotional responses, and empathic processes (Menon & Uddin, 2010). Many deficits observed in BD involve these functions and may be related to insula pathology, such as emotional dysregulation and cognitive impairment. The results of the two meta-analyses converged on the right insula in this study, which showed both spontaneous activity increase and gray matter reduction in BD compared to HCs. Meta-regression analyses indicated that this difference was not significantly affected by age, sex or illness duration. These findings are consistent with results from previous meta-analyses of volumetric measurements in BD (Bora, Fornito, Yuecel, & Pantelis, 2012; Ellison-Wright & Bullmore, 2010; Selvaraj et al., 2012; Wang et al., 2019; Wise et al., 2017; Yu et al., 2019). Previous studies assumed that regional volume changes are associated with changes in glial cell density, neuronal size, and dendritic branching (Anderson, 2011; Rajkowska, 2000; Zaremba et al., 2018), which are known to influence the function of neural circuitries in these regions. Moreover, several brain structural studies found different GMVs in the insular cortex and IFG in individuals at high genetic risk for BD (Kempton et al., 2009; Matsuo et al., 2012; Nery, Monkul, & Lafer, 2013), which suggested that the morphologies of these regions are associated with genetic susceptibility to BD. Similar to our functional results, a recent resting state fMRI meta-analysis also found increased ALFF in the insula extending into the striatum in BD (Gong et al., 2020). Task-based fMRI studies found hypo-activation in the right anterior insula during cognitive control tasks (McTeague et al., 2017). A structural network study reported normalization of altered nodal centralities in the insula after treatment with quetiapine or lithium for six weeks in patients with BD (Lei et al., 2021). Another study found that the left insula increased after lithium treatment in patients with BD (Germana et al., 2010). The bilateral insula is one of the therapeutic targets. After multiple injections of ketamine and cardiac stabilizers, the global functional connectivity density of the bilateral insula in BD patients was reduced and accompanied by relief of depressive symptoms (Zhuo et al., 2020). The activity at the site of stimulation as well as insula increased by transcranial magnetic stimulation (rTMS) in patients with depression (Li et al., 2004; Speer et al., 2000). Although the direction of alteration of the insula is inconsistent across modalities (functional neuroimaging and VBM), previous evidence suggests that increases or reductions in GMV may not directly correspond to functional neural activation or deactivation (Calhoun et al., 2006). A reduction in gray matter could be accompanied by a compensatory hyperfunctionality of the remaining gray matter, which could involve a higher vascularization and thus show as higher spontaneous activation (Radua et al., 2012a). Therefore, the findings of increased activity in the insula could be a compensatory response to structural deficits in BD, which might contribute to the emotional and cognitive impairments of BD.

In this study, neural alterations in the prefrontal cortex were identified in both the functional and structural neuroimaging meta-analyses. Resting-state functional neuroimaging analysis showed increased spontaneous activity in the bilateral ventrolateral prefrontal/orbitofrontal cortex (mainly in the IFG) in BD. In the subgroup analyses, both increased ReHo and ALFF were found in the bilateral ventrolateral prefrontal/orbitofrontal cortex (mainly in the IFG) in BD, suggesting consistency both in the main result and the different functional subgroups. Structural meta-analysis showed decreased GMV in the bilateral mPFC, ACC and IFG in BD. These findings were partially consistent with previous functional(Gong et al., 2019) and structural(Lu et al., 2019; Selvaraj et al., 2012; Wang et al., 2019; Yu et al., 2019) meta-analyses of BD. Postmortem studies showed a reduction in neuronal size and packing density in the lateral prefrontal cortex and orbitofrontal cortex in BD (Rajkowska, 2000). The prefrontal regions are crucial in behavioral and emotional control (Passingham, Toni, & Rushworth, 2000; Phillips, Ladouceur, & Drevets, 2008). In particular, the IFG, which is the ventrolateral part of the prefrontal cortex, plays an important role in executive functions, such as cognitive inhibition(Ganzola & Duchesne, 2017). Task-based fMRI meta-analysis found aberrant activation in the ventrolateral prefrontal regions in BD during emotional processing (McTeague et al., 2020) and cognitive control tasks (McTeague et al., 2017). The ventrolateral prefrontal cortex was shown to be central to affective and non-affective inhibitory control among the same participants, and to show concurrent disruptions in psychopathology (McTeague et al., 2020; Tabibnia et al., 2011). Additionally, our subgroup analysis showed increased spontaneous activity in the bilateral superior frontal gyrus (mainly in the mPFC) in unmedicated patients with BD. These results indicated that abnormal mPFC is not caused by medication effects, mood stabilizers or illness chronicity, further indicating that increased activity in the mPFC is due to primary changes. The mPFC is associated with decision making, more precisely, with risk assessment of choices (Rogers et al., 2004). Muhlert and Lawrence (2015) found that individuals who have smaller volumes of mPFC exhibit riskier behavior during negative emotional states (Muhlert & Lawrence, 2015). Therefore, these findings of gray matter deficits with increased activity in the mPFC may be related to reward hypersensitivity and impaired decision-making in patients with BD (Lu et al., 2019). A previous meta-analysis of structural and functional neuroimaging studies reported increased GMV and activation in the right IFG in unaffected relatives of patients with BD compared with HCs (Cattarinussi, Di Giorgio, Wolf, Balestrieri, & Sambataro, 2019). These results suggested that the IFG difference may be a heritable vulnerability factor for developing BD, which may be necessary but not sufficient to cause the condition. In addition, several studies found that functional activities in the bilateral prefrontal cortex and right orbital frontal cortex were normalized by rTMS treatment in depressed patients (Li et al., 2004; Speer et al., 2000). Taken together, reliable identification of the prefrontal cortex through large-scale multimodal meta-analysis strongly supports this region's role in BD. The abnormalities of the prefrontal gyrus (especially IFG) were found by different methodologies, and may be an early predictor and important target for early intervention in BD.

https://doi.org/10.1017/S0033291722002392 Published online by Cambridge University Press

This study identified increased spontaneous activity in the bilateral striatum (putamen and caudate) and GMV deficits in the left thalamus in BD. In the subgroup analyses, increased ALFF was found in the striatum and thalamus in BD. Consistent with our findings, a recent VBM meta-analysis also reported smaller GMV in the thalamus in euthymic patients with BD relative to HCs (Wang et al., 2019). After lithium treatment, the GMV of the thalamus increased in patients with BD (Abramovic et al., 2016). McDonald and colleagues (McDonald et al., 2004) had reported significant heterogeneity among studies on the thalamus but included fewer studies (26 studies). Several studies have been published since then and we included 83 studies in our meta-analysis. The thalamus plays a key role in the integration and coordination of information as it passes through various brain regions, and its disturbance could explain the resultant psychotic symptoms (Cronenwett & Csernansky, 2010). In addition, previous neuroimaging studies reported increased functional activity (Blumberg et al., 2000), blood flow (He et al., 2019), metabolism (Ketter et al., 2001), and dynamic functional connectivity (Chen et al., 2020a) in the striatum of BD patients. Anatomically, the prefrontal cortex projects heavily to the striatum as part of a circuit that loops through the basal ganglia and thalamus, and then back to the prefrontal cortex (Ding, 2015). Fronto-striatal-thalamic regions and circuitry have been implicated in complex cognitive functions including response inhibition(Morein-Zamir & Robbins, 2015), working memory (Clemensson, Clemensson, Riess, & Huu Phuc, 2017; Darki & Klingberg, 2015), and reward processing(de Leeuw, Kahn, & Vink, 2015). Therefore, these findings, in conjunction with functional and structural changes of the prefrontal cortex, suggest a wider dysfunction of the fronto-striatal-thalamic circuitry, which could result in psychopathological and cognitive symptoms of BD.

The temporal cortex is involved in the processing of auditory information, language comprehension, semantic memory, visual perception, and sensory integration (Selvaraj et al., 2012). Our meta-analysis found decreased spontaneous activity in the left middle temporal gyrus extending to the superior temporal gyrus, and decreased GMV in the bilateral temporal pole extending to the superior temporal gyrus in BD. The subgroup analyses also found decreased ReHo in the left middle temporal gyrus in BD. Previous meta-analyses consistently found reduced GMV in the superior temporal gyrus in patients with BD (Selvaraj et al., 2012; Wang et al., 2019; Wise et al., 2017). Deficits in the superior temporal gyrus are associated with a wide array of symptoms including auditory hallucinations (Barta, Pearlson, Powers, Richards, & Tune, 1990) and errors in facial emotion perception (Hanford, Nazarov, Hall, & Sassi, 2016; Hoffman & Haxby, 2000). Similarly, studies also reported more widespread cortical thinning across the temporal lobes in BD, including the superior, middle and inferior gyri, and temporal pole (Hanford et al., 2016). Functional MRI studies found different activation levels in the superior and middle temporal gyri during emotional processing in BD patients (Mitchell, Elliott, Barry, Cruttenden, & Woodruff, 2004; Pavuluri, O'Connor, Harral, & Sweeney, 2007). Taken together, these findings are consistent with a role of temporal cortex alterations in BD.

This study also found that small parts of some brain regions exhibited either structural or functional changes in BD, such as decreased spontaneous activity in the precuneus and cerebellum, and decreased GMV in the fusiform gyrus extending to the cerebellum. We did not find any significant differences between patients with BD and HCs in lithium subgroup meta-analyses, which may be because patients with BD often take lithium and other mood stabilizers, and GMV is affected by lithium and other mood stabilizers. The precuneus/PCC and mPFC are major hub nodes of the default-mode network (DMN), which is involved in multiple cognitive and affective functions such as emotional processing, self-referential mental activity, distraction and recollection of experiences, and possibly exerts a modulatory role during attention-requiring tasks (Raichle, 2015). Aberrant activity and connectivity within the DMN are well-documented in different mood states of BD (Syan et al., 2018; Vargas et al., 2013; Wang et al., 2020; Zovetti et al., 2020). For example, previous studies found that hypo-connectivity between the anterior and posterior DMN in manic BD patients might be related to an attention pattern that is excessively focused on external stimuli at the expense of internal reflection (Magioncalda et al., 2015; Wang et al., 2020). In contrast, hypo-connectivity within the posterior DMN in depressive BD patients might be related to rumination and working memory impairment (Gong et al., 2019). The cerebellum is known to be connected to cortical areas involved in the pathophysiology of psychiatric disorders such as BD (Lupo, Sicilianob, & Leggio, 2019). Recently, a meta-analysis of VBM studies found decreased cerebellar gray matter in relatives of patients with BD, schizophrenia and major depressive disorder, which suggest that the cerebellum might be associated with shared risk for psychiatric disorders. Studies showed structural and functional alterations in the cerebellum in BD patients during the manic state (Sani et al., 2016; Shaffer et al., 2018), depressed state (Wang et al., 2016; Zhao et al., 2016), and remitted state (Wang et al., 2018b). Taken together, these findings imply that the cerebellum might be a key structure involved in the regulation of mood in BD (Zhang et al., 2020a).

This study had some limitations. First, we could not determine whether these functional and anatomical alterations were part of the pathogenesis or a consequence of these disorders because of the nature of cross-sectional studies. Second, clinical details were often insufficiently reported in the studies for a comprehensive and powerful subgroup or meta-regression analyses. Including a range of clinical variables in future neuroimaging studies would be highly beneficial for future meta-analyses. Relevant clinical information could include bipolar subtype (e.g. I, II, with mainly mixed-episodes, or with psychotic features), mental state (e.g. depressive, manic, and euthymic), rating scale scores, medication status, type of medication administered (e.g. antidepressant, mood stabilizer and antipsychotics) and duration of administration, details of comorbidities, age of onset (geriatric or adolescent BD), disease duration or severity, and number of previous episodes. Third, the method used in this study is based on the peak coordinates and their effect size, rather than the original statistical brain map, which reduced the accuracy of the results (Radua et al., 2012b). Fourth, we used an uncorrected threshold of $p < 0.005$. Although previous studies have shown that the threshold can fully control the false positive rate (Radua et al., 2012b), it is an approximate value of the correction result. After FWE correction, the statistically significant results were significantly reduced. Following reasons may account for the differences: (1) the heterogeneity was not captured in this meta-analysis (e.g. type of medication administered), which may reduce the ability to observe the results after conservative statistical threshold, and (2) case-control studies usually included a small number of cases. Fifth, multimodal analysis conducted in this study did not directly detect correlations between structural and functional differences, but showed brain regions in which BD is associated with structural and functional changes. Future

https://doi.org/10.1017/S0033291722002392 Published online by Cambridge University Press

studies should investigate the spatial and temporal relationships between the structure and function of the brain regions detected in this meta-analysis. Finally, though several studies (Chen et al., 2007; Molina et al., 2011) revealed GMV reductions associated with lithium treatment, only five studies (< 10 studies) compared GMV between BD patients taking lithium and HCs, which did not meet the criteria for subgroup analysis.

In summary, the study findings suggested that BD exhibits similar differences in both function and structure of the insula (extending to the temporal cortex). In addition, fronto-striatal-thalamic and DMN regions exhibited functional or structural differences in BD. These results further expand the growing literature exploring anatomical and functional measures in BD, which provide useful insights for understanding the underlying pathophysiology of BD, and developing more targeted and efficacious treatment and intervention strategies. Further studies were needed with targeted interventions such as TMS therapy on the different brain regions, particularly the insula and prefrontal gyrus.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291722002392

Acknowledgements. The study was supported by grants from the National Natural Science Foundation of China (81671670, 81971597 and 82102003); National Key Research and Development Program of China (2020YFC2005700); Project in Basic Research and Applied Basic Research in General Colleges and Universities of Guangdong, China (2018KZDXM009); Key-Area Research and Development Program of Guangdong Province (2020B1111100001); Medical Science and Technology Research Foundation of Guangdong Province (A2021109). The funding organizations played no further role in study design, data collection, analysis and interpretation and paper writing.

Author contributions. Guanmao Chen: conception and design, acquisition of data, analysis and interpretation of data; drafted the article; gave final approval of the version to be published. Junjing Wang: conception and design, analysis and interpretation of data, gave final approval of the version to be published. Jiaying Gong: analysis and interpretation of data; drafted the article; gave final approval of the version to be published. Zhangzhang Qi: revised the manuscript critically for important intellectual content, gave final approval of the version to be published. Siying Fu: revised the manuscript critically for important intellectual content, gave final approval of the version to be published. Guixian Tang: acquisition of data, gave final approval of the version to be published. Pan Chen: acquisition of data, gave final approval of the version to be published. Li Huang: revised the manuscript critically for important intellectual content, gave final approval of the version to be published. Ying Wang: conception and design, acquisition of data, analysis and interpretation of data; revised the manuscript critically for important intellectual content, gave final approval of the version to be published.

Conflict of interest. The authors declare that they have no conflict of interests.

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

References

Abramovic, L., Boks, M. P. M., Vreeker, A., Bouter, D. C., Kruiper, C., Verkooijen, S., … van Haren, N. E. M. (2016). The association of antipsychotic medication and lithium with brain measures in patients with bipolar disorder. *European Neuropsychopharmacology*, *26*, 1741–1751. doi: 10.1016/j.euroneuro.2016.09.371

Albajes-Eizagirre, A., Solanes, A., & Radua, J. (2019a). Meta-analysis of non-statistically significant unreported effects. *Statistical Methods in Medical Research*, *28*, 3741–3754. doi: 10.1177/0962280218811349

Albajes-Eizagirre, A., Solanes, A., Vieta, E., & Radua, J. (2019b). Voxel-based meta-analysis via permutation of subject images (PSI): Theory and implementation for SDM. *Neuroimage*, *186*, 174–184. doi: 10.1016/j.neuroimage.2018.10.077

Almeida, J. R. C., Akkal, D., Hassel, S., Travis, M. J., Banihashemi, L., Kerr, N., … Phillips, M. L. (2009). Reduced gray matter volume in ventral prefrontal cortex but not amygdala in bipolar disorder: Significant effects of gender and trait anxiety. *Psychiatry Research-Neuroimaging*, *171*, 54–68. doi: 10.1016/j.pscychresns.2008.02.001

Alonso-Lana, S., Goikolea, J. M., Bonnin, C. M., Sarro, S., Segura, B., Amann, B. L., … McKenna, P. J. (2016). Structural and functional brain correlates of cognitive impairment in euthymic patients with bipolar disorder. *Plos One*, *11*, e0158867. doi: 10.1371/journal.pone.0158867

Altamura, A. C., Maggioni, E., Dhanoa, T., Ciappolino, V., Paoli, R. A., Cremaschi, L., … Brambilla, P. (2018). The impact of psychosis on brain anatomy in bipolar disorder: A structural MRI study. *Journal of Affective Disorders*, *233*, 100–109. doi: 10.1016/j.jad.2017.11.092

Ambrosi, E., Rossi-Espagnet, M. C., Kotzalidis, G. D., Comparelli, A., Del Casale, A., Carducci, F., … Girardi, P. (2013). Structural brain alterations in bipolar disorder II: A combined voxel-based morphometry (VBM) and diffusion tensor imaging (DTI) study. *Journal of Affective Disorders*, *150*, 610–615. doi: 10.1016/j.jad.2013.02.023

Anderson, B. J. (2011). Plasticity of gray matter volume: The cellular and synaptic plasticity that underlies volumetric change. *Developmental Psychobiology*, *53*, 456–465. doi: 10.1002/dev.20563

Augustine, J. R. (1996). Circuitry and functional aspects of the insular lobe in primates including humans. *Brain Research Reviews*, *22*, 229–244. doi: 10.1016/s0165-0173(96)00011-2

Barta, P. E., Pearlson, G. D., Powers, R. E., Richards, S. S., & Tune, L. E. (1990). Auditory hallucinations and smaller superior temporal gyral volume in schizophrenia. *The American Journal of Psychiatry*, *147*, 1457–1462.

Bennett, C. M., & Miller, M. B. (2010). How reliable are the results from functional magnetic resonance imaging? *Annals of the New York Academy of Sciences*, *1191*, 133–155. doi: 10.1111/j.1749-6632.2010.05446.x

Biswal, B., Yetkin, F. Z., Haughton, V. M., & Hyde, J. S. (1995). Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. *Magnetic Resonance in Medicine*, *34*, 537–541. doi: 10.1002/mrm.1910340409

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

Bøen, E., Hjørnevik, T., & Hummelen, B. (2019). Patterns of altered regional brain glucose metabolism in borderline personality disorder and bipolar II disorder. *Acta Psychiatrica Scandinavica*, *139*, 256–268. doi: 10.1111/acps.12997

Bora, E., Fornito, A., Yuecel, M., & Pantelis, C. (2012). The effects of gender on grey matter abnormalities in major psychoses: A comparative voxelwise meta-analysis of schizophrenia and bipolar disorder. *Psychological Medicine*, *42*, 295–307. doi: 10.1017/s0033291711001450

Brooks, J. O., Hoblyn, J. C., & Ketter, T. A. (2010). Metabolic evidence of corticolimbic dysregulation in bipolar mania. *Psychiatry Research-Neuroimaging*, *181*, 136–140. doi: 10.1016/j.pscychresns.2009.08.006

Brooks, J. O., Hoblyn, J. C., Woodard, S. A., Rosen, A. C., & Ketter, T. A. (2009). Corticolimbic metabolic dysregulation in euthymic older adults with bipolar disorder. *Journal of Psychiatric Research*, *43*, 497–502. doi: 10.1016/j.jpsychires.2008.08.001

Brown, G. G., Lee, J. S., Strigo, I. A., Caligiuri, M. P., Meloy, M. J., & Lohr, J. (2011). Voxel-based morphometry of patients with schizophrenia or bipolar I disorder: A matched control study. *Psychiatry Research-Neuroimaging*, *194*, 149–156. doi: 10.1016/j.pscychresns.2011.05.005

Bruno, S. D., Barker, G. J., Cercignani, M., Symms, M., & Ron, M. A. (2004). A study of bipolar disorder using magnetization transfer imaging and voxel-based morphometry. *Brain*, *127*, 2433–2440. doi: 10.1093/brain/awh274

Buxton, R. B., Uludağ, K., Dubowitz, D. J., & Liu, T. T. (2004). Modeling the hemodynamic response to brain activation. *Neuroimage*, *23*(Suppl 1), S220–S233. doi: 10.1016/j.neuroimage.2004.07.013

Cai, Y., Liu, J., Zhang, L., Liao, M., Zhang, Y., Wang, L. F., … Li, L. J. (2015). Grey matter volume abnormalities in patients with bipolar I depressive

disorder and unipolar depressive disorder: A voxel-based morphometry study. *Neuroscience Bulletin*, *31*, 4–12. doi: 10.1007/s12264-014-1485-5

Calhoun, V. D., Adali, T., Giuliani, N. R., Pekar, J. J., Kiehl, K. A., & Pearlson, G. D. (2006). Method for multimodal analysis of independent source differences in schizophrenia: Combining gray matter structural and auditory oddball functional data. *Human Brain Mapping*, *27*, 47–62. doi: 10.1002/hbm.20166

Carlisi, C. O., Norman, L. J., Lukito, S. S., Radua, J., Mataix-Cols, D., & Rubia, K. (2017). Comparative multimodal meta-analysis of structural and functional brain abnormalities in autism spectrum disorder and obsessive-compulsive disorder. *Biological Psychiatry*, *82*, 83–102. doi: 10.1016/j.biopsych.2016.10.006

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 Disorders*, *21*, 215–227. doi: 10.1111/bdi.12720

Chen, C. H., Suckling, J., Lennox, B. R., Ooi, C., & Bullmore, E. T. (2011). A quantitative meta-analysis of fMRI studies in bipolar disorder. *Bipolar Disorders*, *13*, 1–15. doi: 10.1111/j.1399-5618.2011.00893.x

Chen, G., Chen, P., Gong, J., Jia, Y., Zhong, S., Chen, F., … Wang, Y. (2020a). Shared and specific patterns of dynamic functional connectivity variability of striato-cortical circuitry in unmedicated bipolar and major depressive disorders. *Psychological Medicine*, *52*, 1–10. doi: 10.1017/s0033291720002378

Chen, M. H., Kao, Z. K., Chang, W. C., Tu, P. C., Hsu, J. W., Huang, K. L., … Bai, Y. M. (2020b). Increased proinflammatory cytokines, executive dysfunction, and reduced gray matter volumes in first-episode bipolar disorder and major depressive disorder. *Journal of Affective Disorders*, *274*, 825–831. doi: 10.1016/j.jad.2020.05.158

Chen, X. H., Wen, W., Malhi, G. S., Ivanovski, B., & Sachdev, P. S. (2007). Regional gray matter changes in bipolar disorder: A voxel-based morphometric study. *Australian and New Zealand Journal of Psychiatry*, *41*, 327–336. doi: 10.1080/00048670701213229

Chen, Z. F., Cui, L. Q., Li, M. L., Jiang, L. J., Deng, W., Ma, X. H., … Li, T. (2012). Voxel-based morphometric and diffusion tensor imaging analysis in male bipolar patients with first-episode mania. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *36*, 231–238. doi: 10.1016/j.pnpbp.2011.11.002

Chen, Z.-Q., Du, M.-Y., Zhao, Y.-J., Huang, X.-Q., Li, J., Lui, S., … Gong, Q.-Y. (2015). Voxel-wise meta-analyses of brain blood flow and local synchrony abnormalities in medication-free patients with major depressive disorder. *Journal of Psychiatry & Neuroscience*, *40*, 401–411. doi: 10.1503/jpn.140119

Clemensson, E. K. H., Clemensson, L. E., Riess, O., & Huu Phuc, N. (2017). The BACHD rat model of Huntington disease shows signs of fronto-striatal dysfunction in two operant conditioning tests of short-term memory. *Plos One*, *12, e0169051*. doi: 10.1371/journal.pone.0169051

Cronenwett, W. J., & Csernansky, J. (2010). Thalamic pathology in schizophrenia. *Current topics in behavioral neurosciences*, *4*, 509–528. doi: 10.1007/7854_2010_55

Cui, L. Q., Li, M. L., Deng, W., Guo, W. J., Ma, X. H., Huang, C. H., … Li, T. (2011). Overlapping clusters of gray matter deficits in paranoid schizophrenia and psychotic bipolar mania with family history. *Neuroscience Letters*, *489*, 94–98. doi: 10.1016/j.neulet.2010.11.073

Darki, F., & Klingberg, T. (2015). The role of fronto-parietal and fronto-striatal networks in the development of working memory: A longitudinal study. *Cerebral Cortex*, *25*, 1587–1595. doi: 10.1093/cercor/bht352

de Leeuw, M., Kahn, R. S., & Vink, M. (2015). Fronto-striatal dysfunction during reward processing in unaffected siblings of schizophrenia patients. *Schizophrenia Bulletin*, *41*, 94–103. doi: 10.1093/schbul/sbu153

Ding, L. (2015). Distinct dynamics of ramping activity in the frontal cortex and caudate nucleus in monkeys. *Journal of Neurophysiology*, *114*, 1850–1861. doi: 10.1152/jn.00395.2015

Eker, C., Simsek, F., Yilmazer, E. E., Kitis, O., Cinar, C., Eker, O. D., … Gonul, A. S. (2014). Brain regions associated with risk and resistance for bipolar I disorder: A voxel-based MRI study of patients with bipolar disorder and their healthy siblings. *Bipolar Disorders*, *16*, 249–261. doi: 10.1111/bdi.12181

Ellison-Wright, I., & Bullmore, E. (2010). Anatomy of bipolar disorder and schizophrenia: A meta-analysis. *Schizophrenia Research*, *117*, 1–12. doi: 10.1016/j.schres.2009.12.022

Frangou, S. (2012). Brain structural and functional correlates of resilience to bipolar disorder. *Frontiers in Human Neuroscience*, *5*, 10. doi: 10.3389/fnhum.2011.00184

Ganzola, R., & Duchesne, S. (2017). Voxel-based morphometry meta-analysis of gray and white matter finds significant areas of differences in bipolar patients from healthy controls. *Bipolar Disorders*, *19*, 74–83. doi: 10.1111/bdi.12488

Germana, C., Kempton, M. J., Sarnicola, A., Christodoulou, T., Haldane, M., Hadjulis, M., … Frangou, S. (2010). The effects of lithium and anticonvulsants on brain structure in bipolar disorder. *Acta Psychiatrica Scandinavica*, *122*, 481–487. doi: 10.1111/j.1600-0447.2010.01582.x

Gong, J., Chen, G., Jia, Y., Zhong, S., Zhao, L., Luo, X., … Wang, Y. (2019). Disrupted functional connectivity within the default mode network and salience network in unmedicated bipolar II disorder. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *88*, 11–18. doi: 10.1016/j.pnpbp.2018.06.012

Gong, J., Wang, J., Qiu, S., Chen, P., Luo, Z., Wang, J., … Wang, Y. (2020). Common and distinct patterns of intrinsic brain activity alterations in major depression and bipolar disorder: Voxel-based meta-analysis. *Translational Psychiatry*, *10*, 353. doi: 10.1038/s41398-020-01036-5

Hajek, T., Alda, M., Hajek, E., & Ivanoff, J. (2013). Functional neuroanatomy of response inhibition in bipolar disorders - combined voxel-based and cognitive performance meta-analysis. *Journal of Psychiatric Research*, *47*, 1955–1966. doi: 10.1016/j.jpsychires.2013.08.015

Hajek, T., Calkin, C., Blagdon, R., Slaney, C., Uher, R., & Alda, M. (2014). Insulin resistance, diabetes mellitus, and brain structure in bipolar disorders. *Neuropsychopharmacology*, *39*, 2910–2918. doi: 10.1038/npp.2014.148

Hajek, T., Cullis, J., Novak, T., Kopecek, M., Hoschl, C., Blagdon, R., … Alda, M. (2012). Hippocampal volumes in bipolar disorders: Opposing effects of illness burden and lithium treatment. *Bipolar Disorders*, *14*, 261–270. doi: 10.1111/j.1399-5618.2012.01013.x

Hanford, L. C., Nazarov, A., Hall, G. B., & Sassi, R. B. (2016). Cortical thickness in bipolar disorder: A systematic review. *Bipolar Disorders*, *18*, 4–18. doi: 10.1111/bdi.12362

He, Z., Sheng, W., Lu, F., Long, Z., Han, S., Pang, Y., … Chen, H. (2019). Altered resting-state cerebral blood flow and functional connectivity of striatum in bipolar disorder and major depressive disorder. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *90*, 177–185. doi: 10.1016/j.pnpbp.2018.11.009

Hoffman, E. A., & Haxby, J. V. (2000). Distinct representations of eye gaze and identity in the distributed human neural system for face perception. *Nature Neuroscience*, *3*, 80–84. doi: 10.1038/71152

Houenou, J., Frommberger, J., Carde, S., Glasbrenner, M., Diener, C., Leboyer, M., & Wessa, M. (2011). Neuroimaging-based markers of bipolar disorder: Evidence from two meta-analyses. *Journal of Affective Disorders*, *132*, 344–355. doi: 10.1016/j.jad.2011.03.016

Kandilarova, S., Stoyanov, D., Sirakov, N., & Maes, M. (2019). Reduced grey matter volume in frontal and temporal areas in depression: Contributions from voxel-based morphometry study. *Acta Neuropsychiatrica*, *31*, 252–257. doi: 10.1016/j.nicl.2020.102220.10.1017/neu.2019.20

Kempton, M. J., Haldane, M., Jogia, J., Grasby, P. M., Collier, D., & Frangou, S. (2009). Dissociable brain structural changes associated with predisposition, resilience, and disease expression in bipolar disorder. *Journal of Neuroscience*, *29*, 10863–10868. doi: 10.1523/jneurosci.2204-09.2009

Ketter, T. A., Kimbrell, T. A., George, M. S., Dunn, R. T., Speer, A. M., Benson, B. E., … Post, R. M. (2001). Effects of mood and subtype on cerebral glucose metabolism in treatment-resistant bipolar disorder. *Biological Psychiatry*, *49*, 97–109. doi: 10.1016/s0006-3223(00)00975-6

Lee, D. K., Lee, H., Park, K., Joh, E., Kim, C. E., & Ryu, S. (2020). Common gray and white matter abnormalities in schizophrenia and bipolar disorder. *PLoS One*, *15*, e0232826. doi: 10.1371/journal.pone.0232826

Lei, D., Li, W., Tallman, M. J., Patino, L. R., McNamara, R. K., Strawn, J. R., … DelBello, M. P. (2021). Changes in the brain structural connectome after a prospective randomized clinical trial of lithium and quetiapine treatment in

https://doi.org/10.1017/S0033291722002392 Published online by Cambridge University Press

youth with bipolar disorder. *Neuropsychopharmacology*, *46*, 1315–1323. doi: 10.1038/s41386-021-00989-5

Li, H., Cui, L., Cao, L., Zhang, Y., Liu, Y., Deng, W., & Zhou, W. (2020). Identification of bipolar disorder using a combination of multimodality magnetic resonance imaging and machine learning techniques. *BMC Psychiatry*, *20*, 488. doi: 10.1186/s12888-020-02886-5

Li, M. L., Cui, L. Q., Deng, W., Ma, X. H., Huang, C. H., Jiang, L. J., … Li, T. (2011). Voxel-based morphometric analysis on the volume of gray matter in bipolar I disorder. *Psychiatry Research-Neuroimaging*, *191*, 92–97. doi: 10.1016/j.pscychresns.2010.09.006

Li, X. B., Nahas, Z., Kozel, F. A., Anderson, B., Bohning, D. E., & George, M. S. (2004). Acute left prefrontal transcranial magnetic stimulation in depressed patients is associated with immediately increased activity in prefrontal cortical as well as subcortical regions. *Biological Psychiatry*, *55*, 882–890. doi: 10.1016/j.biopsych.2004.01.017

Liu, C. H., Li, F., Li, S. F., Wang, Y. J., Tie, C. L., Wu, H. Y., … Wang, C. Y. (2012a). Abnormal baseline brain activity in bipolar depression: A resting-state functional magnetic resonance imaging study. *Psychiatry Research – Neuroimaging*, *203*, 175–179. doi: 10.1016/j.pscychresns.2012.02.007…

Liu, C. H., Ma, X., Li, F., Wang, Y. J., Tie, C. L., Li, S. F., … Wang, C. Y. (2012b). Regional homogeneity within the default mode network in bipolar depression: A resting-state functional magnetic resonance imaging study. *Plos One*, *7*, e48181. doi: 10.1371/journal.pone.0048181

Liu, F., Zhuo, C., & Yu, C. (2016). Altered cerebral blood flow covariance network in schizophrenia. *Frontiers in Neuroscience*, *10*, 308. doi: 10.3389/fnins.2016.00308

Lu, X., Zhong, Y., Ma, Z., Wu, Y., Fox, P. T., Zhang, N., & Wang, C. (2019). Structural imaging biomarkers for bipolar disorder: Meta-analyses of whole-brain voxel-based morphometry studies. *Depression and Anxiety*, *36*, 353–364. doi: 10.1002/da.22866

Lupo, M., Sicilianob, L., & Leggio, M. (2019). From cerebellar alterations to mood disorders: A systematic review. *Neuroscience and Biobehavioral Reviews*, *103*, 21–28. doi: 10.1016/j.neubiorev.2019.06.008

Magioncalda, P., Martino, M., Conio, B., Escelsior, A., Piaggio, N., Presta, A., … Amore, M. (2015). Functional connectivity and neuronal variability of resting state activity in bipolar disorder-reduction and decoupling in anterior cortical midline structures. *Human Brain Mapping*, *36*, 666–682. doi: 10.1002/hbm.22655

Matsuo, K., Kopecek, M., Nicoletti, M. A., Hatch, J. P., Watanabe, Y., Nery, F. G., … Soares, J. C. (2012). New structural brain imaging endophenotype in bipolar disorder. *Molecular Psychiatry*, *17*, 412–420. doi: 10.1038/mp.2011.3

McCarthy, M. J., Liang, S., Spadoni, A. D., Kelsoe, J. R., & Simmons, A. N. (2014). Whole brain expression of bipolar disorder associated genes: Structural and genetic analyses. *PLoS ONE*, *9*, e100204. doi: 10.1371/journal.pone.0100204

McDonald, C., Zanelli, J., Rabe-Hesketh, S., Ellison-Wright, I., Sham, P., Kalidindi, S., … Kennedy, N. (2004). Meta-analysis of magnetic resonance imaging brain morphometry studies in bipolar disorder. *Biological Psychiatry*, *56*, 411–417. doi: 10.1016/j.biopsych.2004.06.021

McTeague, L. M., Huemer, J., Carreon, D. M., Jiang, Y., Eickhoff, S. B., & Etkin, A. (2017). Identification of common neural circuit disruptions in cognitive control across psychiatric disorders. *American Journal of Psychiatry*, *174*, 676–685. doi: 10.1176/appi.ajp.2017.16040400

McTeague, L. M., Rosenberg, B. M., Lopez, J. W., Carreon, D. M., Huemer, J., Jiang, Y., … Etkin, A. (2020). Identification of common neural circuit disruptions in emotional processing across psychiatric disorders. *American Journal of Psychiatry*, *177*, 411–421. doi: 10.1176/appi.ajp.2019.18111271

Menon, V., & Uddin, L. Q. (2010). Saliency, switching, attention and control: A network model of insula function. *Brain Structure & Function*, *214*, 655–667. doi: 10.1007/s00429-010-0262-0

Merikangas, K. R., Akiskal, H. S., Angst, J., Greenberg, P. E., Hirschfeld, R. M. A., Petukhova, M., & Kessler, R. C. (2007). Lifetime and 12-month prevalence of bipolar spectrum disorder in the national comorbidity survey replication. *Archives of General Psychiatry*, *64*, 543–552. doi: 10.1001/archpsyc.64.5.543

Mitchell, R. L. C., Elliott, R., Barry, M., Cruttenden, A., & Woodruff, P. W. R. (2004). Neural response to emotional prosody in schizophrenia and in bipolar affective disorder. *British Journal of Psychiatry*, *184*, 223–230. doi: 10.1192/bjp.184.3.223

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Open Medicine*, *3*, e123–e130.

Molina, V., Galindo, G., Cortés, B., de Herrera, A. G., Ledo, A., Sanz, J., … Hernández-Tamames, J. A. (2011). Different gray matter patterns in chronic schizophrenia and chronic bipolar disorder patients identified using voxel-based morphometry. *European Archives of Psychiatry and Clinical Neuroscience*, *261*, 313–322. doi: 10.1007/s00406-010-0183-1

Morein-Zamir, S., & Robbins, T. W. (2015). Fronto-striatal circuits in response-inhibition: Relevance to addiction. *Brain Research*, *1628*, 117–129. doi: 10.1016/j.brainres.2014.09.012

Muhlert, N., & Lawrence, A. D. (2015). Brain structure correlates of emotion-based rash impulsivity. *Neuroimage*, *115*, 138–146. doi: 10.1016/j.neuroimage.2015.04.061

Nery, F. G., Monkul, E. S., & Lafer, B. (2013). Gray matter abnormalities as brain structural vulnerability factors for bipolar disorder: A review of neuroimaging studies of individuals at high genetic risk for bipolar disorder. *Australian and New Zealand Journal of Psychiatry*, *47*, 1124–1135. doi: 10.1177/0004867413496482

Oertel-Knochel, V., Reinke, B., Feddern, R., Knake, A., Knochel, C., Prvulovic, D., … Linden, D. E. J. (2014). Episodic memory impairments in bipolar disorder are associated with functional and structural brain changes. *Bipolar Disorders*, *16*, 830–845. doi: 10.1111/bdi.12241

Passingham, R. E., Toni, I., & Rushworth, M. F. S. (2000). Specialisation within the prefrontal cortex: The ventral prefrontal cortex and associative learning. *Experimental Brain Research*, *133*, 103–113. doi: 10.1007/s002210000405

Pavuluri, M. N., O'Connor, M. M., Harral, E., & Sweeney, J. A. (2007). Affective neural circuitry during facial emotion processing in pediatric bipolar disorder. *Biological Psychiatry*, *62*, 158–167. doi: 10.1016/j.biopsych.2006.07.011

Phillips, M. L., Ladouceur, C. D., & Drevets, W. C. (2008). A neural model of voluntary and automatic emotion regulation: Implications for understanding the pathophysiology and neurodevelopment of bipolar disorder. *Molecular Psychiatry*, *13*, 833–857. doi: 10.1038/mp.2008.65

Qiu, M., Zhang, H., Mellor, D., Shi, J., Wu, C., Huang, Y., … Peng, D. (2018). Aberrant neural activity in patients with bipolar depressive disorder distinguishing to the unipolar depressive disorder: A resting-state functional magnetic resonance imaging study. *Frontiers in Psychiatry*, *9*, 238. doi: 10.3389/fpsyt.2018.00238

Radua, J., Borgwardt, S., Crescini, A., Mataix-Cols, D., Meyer-Lindenberg, A., McGuire, P. K., & Fusar-Poli, P. (2012a). Multimodal meta-analysis of structural and functional brain changes in first episode psychosis and the effects of antipsychotic medication. *Neuroscience and Biobehavioral Reviews*, *36*, 2325–2333. doi: 10.1016/j.neubiorev.2012.07.012

Radua, J., & Mataix-Cols, D. (2009). Voxel-wise meta-analysis of grey matter changes in obsessive-compulsive disorder. *British Journal of Psychiatry*, *195*, 393–402. doi: 10.1192/bjp.bp.108.055046

Radua, J., Mataix-Cols, D., Phillips, M. L., El-Hage, W., Kronhaus, D. M., Cardoner, N., & Surguladze, S. (2012b). A new meta-analytic method for neuroimaging studies that combines reported peak coordinates and statistical parametric maps. *European Psychiatry*, *27*, 605–611. doi: 10.1016/j.eurpsy.2011.04.001

Raichle, M. E. (2015). The brain's default mode network. *Annual review of neuroscience*, *38*, 433-447. doi: 10.1146/annurev-neuro-071013-014030

Rajkowska, G. (2000). Postmortem studies in mood disorders indicate altered numbers of neurons and glial cells. *Biological Psychiatry*, *48*, 766–777. doi: 10.1016/s0006-3223(00)00950-1

Rogers, R. D., Ramnani, N., Mackay, C., Wilson, J. L., Jezzard, P., Carter, C. S., & Smith, S. M. (2004). Distinct portions of anterior cingulate cortex and medial prefrontal cortex are activated by reward processing in separable phases of decision-making cognition. *Biological Psychiatry*, *55*, 594–602. doi: 10.1016/j.biopsych.2003.11.012

Sani, G., Chiapponi, C., Piras, F., Ambrosi, E., Simonetti, A., Danese, E., … Spalletta, G. (2016). Gray and white matter trajectories in patients with bipolar disorder. *Bipolar Disorders*, *18*, 52–62. doi: 10.1111/bdi.12359

https://doi.org/10.1017/S0033291722002392 Published online by Cambridge University Press

Selvaraj, S., Arnone, D., Job, D., Stanfield, A., Farrow, T. F. D., Nugent, A. C., … McIntosh, A. M. (2012). Grey matter differences in bipolar disorder: A meta-analysis of voxel-based morphometry studies. *Bipolar Disorders*, *14*, 135–145. doi: 10.1111/j.1399-5618.2012.01000.x…

Shaffer, Jr. J. J., Johnson, C. P., Fiedorowicz, J. G., Christensen, G. E., Wemmie, J. A., & Magnotta, V. A. (2018). Impaired sensory processing measured by functional MRI in bipolar disorder manic and depressed mood states. *Brain Imaging and Behavior*, *12*, 837–847. doi: 10.1007/s11682-017-9741-8

Shepherd, A. M., Matheson, S. L., Laurens, K. R., Carr, V. J., & Green, M. J. (2012). Systematic meta-analysis of insula volume in schizophrenia. *Biological Psychiatry*, *72*, 775–784. doi: 10.1016/j.biopsych.2012.04.020

Smith, S. M., & Nichols, T. E. (2009). Threshold-free cluster enhancement: Addressing problems of smoothing, threshold dependence and localisation in cluster inference. *Neuroimage*, *44*, 83–98. doi: 10.1016/j.neuroimage.2008.03.061

Speer, A. M., Kimbrell, T. A., Wassermann, E. M., Repella, J. D., Willis, M. W., Herscovitch, P., & Post, R. M. (2000). Opposite effects of high and low-frequency rTMS on regional brain activity in depressed patients. *Biological Psychiatry*, *48*, 1133–1141. doi: 10.1016/s0006-3223(00)01065-9

Stroup, D. F., Berlin, J. A., Morton, S. C., Olkin, I., Williamson, G. D., Rennie, D., … Grp, M. (2000). Meta-analysis of observational studies in epidemiology: A proposal for reporting. *Jama-Journal of the American Medical Association*, *283*, 2008–2012. doi: 10.1001/jama.283.15.2008

Sun, N., Li, Y., Zhang, A., Yang, C., Liu, P., Liu, Z., … Zhang, K. (2020). Fractional amplitude of low-frequency fluctuations and gray matter volume alterations in patients with bipolar depression. *Neuroscience Letters*, *730*, 135030. doi: 10.1016/j.neulet.2020.135030

Syan, S. K., Smith, M., Frey, B. N., Remtulla, R., Kapczinski, F., Hall, G. B. C., & Minuzzi, L. (2018). Resting-state functional connectivity in individuals with bipolar disorder during clinical remission: A systematic review. *Journal of Psychiatry & Neuroscience*, *43*, 298–316. doi: 10.1503/jpn.170175

Tabibnia, G., Monterosso, J. R., Baicy, K., Aron, A. R., Poldrack, R. A., Chakrapani, S., … London, E. D. (2011). Different forms of self-control share a neurocognitive substrate. *Journal of Neuroscience*, *31*, 4805–4810. doi: 10.1523/jneurosci.2859-10.2011

Toma, S., MacIntosh, B. J., Swardfager, W., & Goldstein, B. I. (2018). Cerebral blood flow in bipolar disorder: A systematic review. *Journal of Affective Disorders*, *241*, 505–513. doi: 10.1016/j.jad.2018.08.040

Vai, B., Parenti, L., Bollettini, I., Cara, C., Verga, C., Melloni, E., … Benedetti, F. (2020). Predicting differential diagnosis between bipolar and unipolar depression with multiple kernel learning on multimodal structural neuroimaging. *European Neuropsychopharmacology*, *34*, 28–38. doi: 10.1016/j.euroneuro.2020.03.008

Vargas, C., Lopez-Jaramillo, C., & Vieta, E. (2013). A systematic literature review of resting-state network-functional MRI in bipolar disorder. *Journal of Affective Disorders*, *150*, 727–735. doi: 10.1016/j.jad.2013.05.083

Wang, X., Luo, Q., Tian, F., Cheng, B., Qiu, L., Wang, S., … Jia, Z. (2019). Brain grey-matter volume alteration in adult patients with bipolar disorder under different conditions: A voxel-based meta-analysis. *Journal of Psychiatry & Neuroscience*, *44*, 89–101. doi: 10.1503/jpn.180002

Wang, X., Tian, F., Wang, S., Cheng, B., Qiu, L., He, M., … Jia, Z. (2018a). Gray matter bases of psychotic features in adult bipolar disorder: A systematic review and voxel-based meta-analysis of neuroimaging studies. *Human Brain Mapping*, *39*, 4707–4723. doi: 10.1002/hbm.24316

Wang, Y., Gao, Y., Tang, S., Lu, L., Zhang, L., Bu, X., … 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. doi: 10.1016/j.ebiom.2020.102742

Wang, Y., Zhong, S., Chen, G., Liu, T., Zhao, L., Sun, Y., … Huang, L. (2018b). Altered cerebellar functional connectivity in remitted bipolar disorder: A resting-state functional magnetic resonance imaging study. *Australian and New Zealand Journal of Psychiatry*, *52*, 962–971. doi: 10.1177/0004867417745996

Wang, Y., Zhong, S., Jia, Y., Sun, Y., Wang, B., Liu, T., … Huang, L. (2016). Disrupted resting-state functional connectivity in nonmedicated bipolar disorder. *Radiology*, *280*, 529–536. doi: 10.1148/radiol.2016151641

Wise, T., Radua, J., Via, E., Cardoner, N., Abe, O., Adams, T. M., … Arnone, D. (2017). Common and distinct patterns of grey-matter volume alteration in major depression and bipolar disorder: Evidence from voxel-based meta-analysis. *Molecular Psychiatry*, *22*, 1455–1463. doi: 10.1038/mp.2016.72

Xu, K., Liu, H., Li, H., Tang, Y., Womer, F., Jiang, X., … Wang, F. (2014a). Amplitude of low-frequency fluctuations in bipolar disorder: A resting-state fMRI study. *Journal of Affective Disorders*, *152–154*, 237–242. doi: 10.1016/j.jad.2013.09.017…

Yu, H., Meng, Y.-J., Li, X.-J., Zhang, C., Liang, S., Li, M.-L., … Li, T. (2019). Common and distinct patterns of grey matter alterations in borderline personality disorder and bipolar disorder: Voxel-based meta-analysis. *British Journal of Psychiatry*, *215*, 395–403. doi: 10.1192/bjp.2019.44

Zaremba, D., Dohm, K., Redlich, R., Grotegerd, D., Strojny, R., Meinert, S., … Dannlowski, U. (2018). Association of brain cortical changes with relapse in patients with major depressive disorder. *Jama Psychiatry*, *75*, 484–492. doi: 10.1001/jamapsychiatry.2018.0123

Zhang, K., Liu, Z., Cao, X., Yang, C., Xu, Y., Xu, T., … Yang, Z. (2017). Amplitude of low-frequency fluctuations in first-episode, drug-naïve depressive patients: A 5-year retrospective study. *Plos One*, *12*, e0174564. doi: 10.1371/journal.pone.0174564

Zhang, W., Sweeney, J. A., Yao, L., Li, S., Zeng, J., Xu, M., & Tallman, M. J. (2020a). Brain structural correlates of familial risk for mental illness: A meta-analysis of voxel-based morphometry studies in relatives of patients with psychotic or mood disorders. *45*, 1369–1379. doi: 10.1038/s41386-020-0687-y

Zhang, Z., Bo, Q., Li, F., Zhao, L., Wang, Y., Liu, R., … Zhou, Y. (2020b). Increased ALFF and functional connectivity of the right striatum in bipolar disorder patients. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *111*, 110140. doi: 10.1016/j.pnpbp.2020.110140

Zhao, L., Wang, Y., Jia, Y., Zhong, S., Sun, Y., Zhou, Z., … Huang, L. (2016). Cerebellar microstructural abnormalities in bipolar depression and unipolar depression: A diffusion kurtosis and perfusion imaging study. *Journal of Affective Disorders*, *195*, 21–31. doi: 10.1016/j.jad.2016.01.042

Zhuo, C., Ji, F., Tian, H., Wang, L., Jia, F., Jiang, D., … Zhu, J. (2020). Transient effects of multi-infusion ketamine augmentation on treatment-resistant depressive symptoms in patients with treatment-resistant bipolar depression - An open-label three-week pilot study. *Brain and Behavior*, *10*, e01674. doi: 10.1002/brb3.1674

Zovetti, N., Rossetti, M. G., Perlini, C., Maggioni, E., Bontempi, P., Bellani, M., … Brambilla, P. (2020). Default mode network activity in bipolar disorder. *Epidemiology and Psychiatric Sciences*, *29*, e166. doi: 10.1017/s2045796020000803

https://doi.org/10.1017/S0033291722002392 Published online by Cambridge University Press