

Supplemental Online Content

Mesbah R, Koenders MA, Van der Wee NJA, Giltay EJ, van Hemert AM, de Leeuw M. Association between the fronto-limbic network and cognitive and emotional functioning in individuals with bipolar disorder: a systematic review and meta-analysis. *JAMA Psychiatry*. Published online March 29, 2023.
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This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods. Literature search

The literature search included all the fMRI studies on BD before March 2020. An independent employee of the Walaeus Library (Leiden University Libraries) performed the literature search. The authors screened first for eligibility based on titles and abstracts according to the inclusion and exclusion criteria. When this was unclear, the full-text review was carried out. The full-text of the remaining studies was beside the authors reviewed independently by two interns in the field of psychology. Disagreements were managed by discussion to reach a consensus.

We used the following key words (using both free-text and MeSH search):

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("fMRI"[tw] OR "f mri"[tw] OR fmr imag*[tw] OR functional magnetic*[tw] OR "functional magnetic resonance imaging"[tw] OR "functional mri"[tw] OR "functional mr"[tw] OR ("Magnetic Resonance Imaging"[mesh] AND "functional"[tw]) OR ("Magnetic Resonance Imaging"[mesh] OR MR imag*[tw] OR "MRI"[tw] OR "magnetic resonance"[tw])) AND ("Functional Neuroimaging"[Mesh:noexp] OR functional imag*[tw] OR functional neuroimag*[tw])) AND ("Bipolar Disorder"[Mesh] OR "Bipolar and Related Disorders"[Mesh] OR "Bipolar Disorder"[tw] OR "Bipolar Disorders"[tw] OR "Manic-Depressive Psychosis"[tw] OR "Manic Depressive Psychosis"[tw] OR "Bipolar Affective Psychosis"[tw] OR "Manic-Depressive Psychoses"[tw] OR "Mania"[tw] OR "Manias"[tw] OR "Manic State"[tw] OR "Manic States"[tw] OR "Bipolar Depression"[tw] OR "Manic Disorder"[tw] OR "Manic Disorders"[tw] OR "manic depressive"[tw] OR "manic"[tw] OR Bipolar affectiv*[tw] OR Bipolar disease*[tw] OR Bipolar disorder*[tw] OR bipolar depress*[tw]) NOT ("Animals"[mesh] NOT "Humans"[mesh])
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eTable 1. PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	It is reported as meta-analysis in the title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	See abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	4-5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	4-5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	See Appendix
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	See Appendix
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	See Appendix
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	See Appendix
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	6-7
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	6-7
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	N/A
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	N/A

Section and Topic	Item #	Checklist item	Location where item is reported
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	6
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	N/A
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	6-7
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	Table 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	N/A
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table 3 and 4
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	N/A
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Table 2 and 3
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	8-9
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	8-9

Section and Topic	Item #	Checklist item	Location where item is reported
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	10
	23b	Discuss any limitations of the evidence included in the review.	10-14
	23c	Discuss any limitations of the review processes used.	13
	23d	Discuss implications of the results for practice, policy, and future research.	13
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	the review was not registered
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Protocols of BrainMap* were used.
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	N/A
Competing interests	26	Declare any competing interests of review authors.	15
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	15

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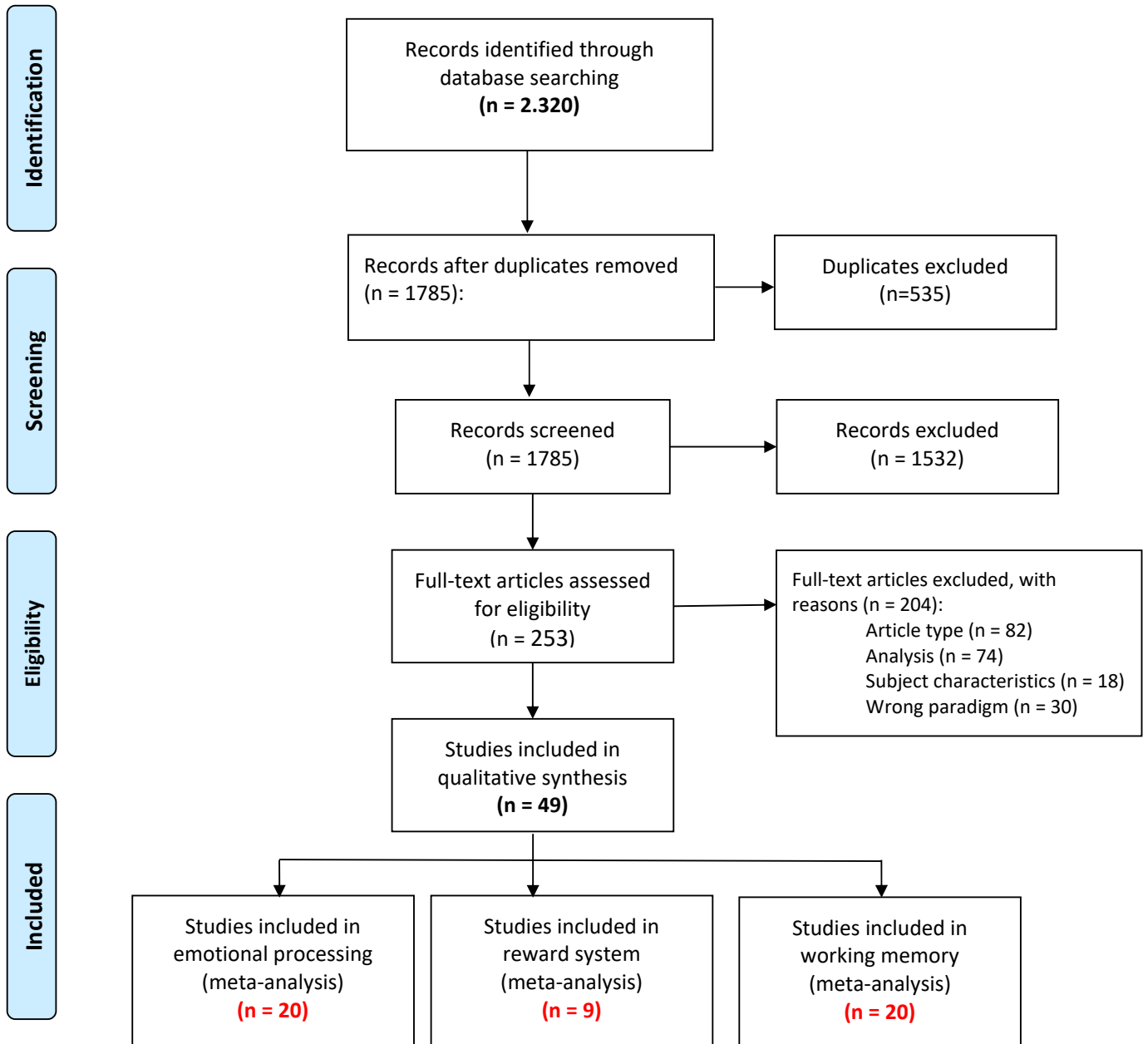
For more information, visit: <http://www.prisma-statement.org/>

* Fox PT, Lancaster JL. Mapping context and content: The BrainMap model. *Nature Rev Neurosci* 3, 319-321, 2002.

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eFigure 1. PRISMA Flow chart

PRISMA flow chart of the literature search for included studies.



eTable 2. Descriptives of included fMRI studies of three domains of emotion processing, reward processing and working memory in the meta-analysis using a whole-brain approach. A total of 46 papers has been used including 49 fMRI studies.

Emotion Tasks					Mood states	Medication	Task	
	BD patients (n) (female, %)	BD type I or II (n)	HC (n) (female, %)	BD patients (mean age, SD)	HC (mean age, SD)	Mood Stabilizers (n) Antipsychotics (n) Antidepressants (n)		
(Cerullo et al. 2014) ¹	25, 68%	BD I (25)	25, 67%	30.0 (8.0)	26.0 (7.0)	Depressed (n = 25)	Unmedicated (25)	Modified continuous performance task emotional and neutral distracters (CPT-END)
(Mitchell et al. 2004) ²	11, 0%	BD NS (11)	13, 0%	42.8 (1.8)	32,2 (3.6)	Not specified (n = 11)	MS (9), AP (4), AD (5)	Emotional prosody task
(Wessa et al. 2007) ³	17, 41%	BD I (10), BD II (7)	17, 35%	44.9 (12.7)	44.9 (13.4)	Euthymic (n = 17)	MS (7), AP (8)	Affective go/no-go task
(Whalley et al. 2009) ⁴	14, 29%	BD I (14)	14, 26%	35.4 (8.4)	38.4 (10.0)	Not specified (n = 14)	MS (4), AP (8), AD (3)	Emotional memory task
(Young, Bodurka, and Drevets 2016) ⁵	16, 88%	BD I (16)	16, 88%	37.6 (9.3)	37.8 (8.7)	Depressed (n = 16)	Unmedicated (16)	Emotional autobiographical memory task
(Morris et al. 2012) ⁶	13, 38%	BD I (13)	15, 60%	41.0 (3.0)	35.0 (2.0)	Euthymic (n = 6) Hypomanic (n = 5) Not specified (n = 2)	AP (5), AD (6)	Emotion regulation task
(Zhang et al. 2020) ⁷	15, 33%	BD I (13), BD II (2)	15, 60%	39.9 (12.5)	33.6 (11.1)	Depressed (n = 2) Not specified (n = 13)	AP (15), AD (9)	Emotion regulation task
(Han et al. 2018) ⁸	10, 40%	BD I (10)	10, 40%	38.6 (9.4)	31.8 (8.0)	Euthymic (n = 10)	MS (10), AD (8)	Emotional picture task
(Moser et al. 2018) ⁹	37, 32%	BD I (37)	48, 42%	27.5 (8.1)	29.8 (8.5)	Not specified (n = 27)	MS (15), AP (30), AD (7)	Emotion recognition task
(Kryza-Lacombe et al. 2019) ¹⁰	33, 78%	BD I (21), BD II (11)	22, 55%	38.2 (11.1)	29.4 (7.2)	Depressed (n = 8) Hypomanic (n = 4) Mixed (n = 1) Euthymic (n = 44)	MS (29), AP (18), AD (15)	Face emotion labelling task
(Elliott et al. 2004) ¹¹	8, 50%	BD I (7), BD II (1)	11, 73%	35.0 (-)	37.6 (9.7)	Manic (n = 8)	MS (7), AP (5)	Affective go/no-go task
(Foland et al. 2008) ¹²	9, 66%	BD I (9)	9, 66%	34.6 (8.0)	30.4 (7.6)	Manic (n = 9)	MS (8), AP (1)	Face emotion labelling task
(Lennox et al. 2004) ¹³	10, 20%	BD I (10)	12, 50%	37.3 (12.8)	32.6 (10.7)	Manic (n = 10)	MS (10), AP (8)	Face emotion labelling task
(Malhi et al. 2007) ¹⁴	10, 100 %	BD I (10)	10, 100%	33.5 (8.7)	33.6 (6.4)	Euthymic (n = 10)	MS (7)	Explicit facial emotion recognition task

(Altshuler et al. 2008) ¹⁵	11, 54%	BD I (11)	17, 47%	32.0 (7.3)	29.5 (6.6)	Depressed (n = 11)	MS (8), AP (2), AD (3)	Face-matching task
(Chen et al. 2006) ¹⁶	16, 19%	BD I (16)	8, 75%	Manic = 39 (13.4) Depressed = 41.9 (12.1)	38.75 (12.5)	Manic (n = 8) Depressed (n = 8)	MS (16), AP (6), AD (2)	Explicit and implicit face recognition task
(Jogia et al. 2008) ¹⁷	12, 58%	BD I (12)	12, 58%	42.1 (11.8)	41.8 (10.9)	Not specified (n = 12)	MS (12)	Sad affect face recognition task
(Hassel et al. 2008) ¹⁸	19, 52%	BD I (19)	24, 54%	32.5 (8.8)	27.7 (8.7)	Euthymic (n = 19)	MS (12), AP (14), AD (9)	Facial expression task
(Killgore, Gruber, and Yurgelun-Todd 2008) ¹⁹	14, 21%	BD NS (14)	13, 8%	28.1 (11.2)	25.5 (4.7)	Not specified (n = 14)	MS (5), AP (12), AD (1)	Fearful face perception task
(Lagopoulos and Malhi 2007) ²⁰	10, 100%	BD I (10)	10, 100%	33.6 (8.12)	33.6 (6.7)	Euthymic (n = 10)	MS (7)	Emotional Stroop task
Reward Tasks								
(Abler et al. 2008) ²¹	12, 41.7%	BD I (12)	12, 41.7%	33.9 (11.2)	36.2 (11.2)	Manic (n = 8) Mixed (n = 3) Hypomanic (n = 1)	MS (12)	Monetary incentive task
(Caseras et al. 2013) ²²	32, 59%	BD I (17), BD II (15)	20, 65%	42.3 (6.0)	41.6 (7.7)	Hypomanic (n = 1) Euthymic (n = 31)	MS (22), AP (12), AD (12)	Monetary reward processing task
(Chase et al. 2013) ²³	23, 82%	BD I (23)	37, 67%	33.9 (8.5)	33.1 (6.2)	Depressed (n = 25)	MS (13), AP (11), AD (9)	Card number guessing task
(Frangou et al. 2008) ²⁴	7, 71%	BD I (7)	7, 71%	37.0 (5.9)	39.0 (5.9)	Euthymic (n = 7)	MS (7)	Gambling task
(Jogia et al. 2012) ²⁵	36, 53%	BD I (36)	37, 43%	42.5 (10.6)	37.6 (11.3)	Euthymic (n = 36)	Unmedicated (14) A (21), AP (6), AD (7)	Iowa gambling task
(Kirschner et al. 2019) ²⁶	25, 36%	BD I (25)	25, 36%	37.3 (9.1)	33.1 (9.7)	Euthymic (n = 25)	MS (18), AP (18), AD (7)	Monetary incentive delayed task
(Manelis et al. 2019) ²⁷	34, 85%	BD I (34)	17, 59%	35.1 (1.3)	31.4 (1.5)	Depressed (n = 16) Euthymic (n = 18)	MS (10), AP (19), AD (15)	Card number guessing task
(Mason et al. 2014) ²⁸	20, 50%	BD I (18), BD II (2)	20, 55%	36.0 (4.3)	33.25 (9.3)	Euthymic (n = 20)	MS (8)	Roulette task
(Sharma et al. 2016) ²⁹	24, 58%		30, 55%	38.0 (11.7)	39.4 (11.8)	Depressed (n = 24)	MS (11), AP (11), AD (6)	Monetary reward procedure
Working Memory Tasks								
(Adler et al. 2004) ³⁰	15, unknown	BD I (15)	15, unknown	29.0 (9.0)	30.0 (9.0)	Euthymic (n = 15)	Unmedicated (4) Unknown (11)	Letter n-back task
(Brooks et al. 2015) ³¹	19, 42%	BD II (19)	19, 52%	36.7 (11.4)	42.6 (12.0)	Depressed (n = 19)	Unmedicated (19)	Letter n-back task
(Deckersbach et al. 2008) ³²	9, 100%	BD I (9)	17, 100%	27.6 (2.8)	25.6 (5.9)	Depressed (n = 9)	MS (9)	Letter n-back task (with mood induction)
(Drapier et al. 2008) ³³	20, 45%	BD I (20)	20, 50%	42.7 (10.4)	41.9 (11.6)	Euthymic (n = 20)	MS (16), AP (4), AD (2)	Letter n-back tasks
(Fernández-Corcuera et al. 2013) ³⁴	41, 45%	BD NS (41)	41, 41%	40.4 (10.2)	40.3 (9.8)	Depressed (n = 41)	Unmedicated (41)	Letter n-back task

(Frangou et al. 2008) ²⁴	7, 71%	BD I (7)	7, 71%	37.0 (5.9)	39.0 (5.9)	Euthymic (n = 7)	MS (7)	Letter n-back task
(Gruber et al. 2010) ³⁵	18, 44%	BD I (18)	18, 61%	38.2 (9.9)	33.9 (11.5)	Euthymic (n = 18)	Unmedicated (3) MS (12), AP (3), AD (6)	Verbal delayed-match-to-sample task
(Hamilton et al. 2009) ³⁶	21, 38%	BD I (21)	38, 39%	36.4 (10.7)	32.5 (11.7)	Euthymic (n = 21)		Delayed match to sample task
(Jogia et al. 2012) ²⁵	36, 53%	BD I (36)	37, 43%	42.5 (10.6)	37.6 (11.3)	Euthymic (n = 36)	Unmedicated (14) MS (21), AP (6), AD (7)	Letter n-back task
(Lagopoulos, Ivanovski, and Malhi 2007) ³⁷	10, 100%	BD I (10)	10, 100%	32.4 (10.8)	31.7 (11.9)	Euthymic (n = 10)	MS (7)	Delay-response memory task
(McKenna et al. 2014) ³⁸	23, 65%	BD I (23)	23, 65%	45.3 (9.5)	44.8 (10.6)	Euthymic (n = 23)	MS (17), AP (12), AD (11)	Pseudoword delayed match to sample task
(Monks et al. 2004) ³⁹	12, 100%	BD I (12)	12, 100%	45.8 (3.5)	45.6 (3.5)	Euthymic (n = 12)	MS (12)	Letter n-back task Sternberg task
(Pomarol-Clotet et al. 2012) ⁴⁰	29, 37%	BD I (29)	46, 41%	49.8 (12.1)	36.3 (13.6)	Manic (n = 29)	MS (23), AP (24)	Letter n-back task
(Pomarol-Clotet et al. 2015) ⁴¹	114, 54%	BD I (108), BD II (6)	38, 52%	39.9 (10.2)	39.7 (8.9)	Manic (n = 38) Depressed (n = 38) Euthymic (n = 38)	MS (95), AP (69), AD (32)	Letter n-back task
(Robinson et al. 2009) ⁴²	15, 53%	BD I (15)	15, 47%	39.0 (12.6)	36.2 (10.6)	Euthymic (n = 15)	MS (8), AP (7), AD (12)	Delayed-non-match-to-sample task
(Wu et al. 2014) ⁴³	20, 52%	BD I (20)	29, 50%	27.9 (6.4)	22.7 (5.1)	Not specified (n = 20)	MS (18), AP (7), AD (12)	Letter n-back task
(Rodríguez-Cano et al. 2017) ⁴⁴	26, 61%	BD I (26)	26, 61%	45.6 (9.2)	46.8 (11.2)	Depressed (n = 26)	MS (23), AP (14), AD (15)	Letter n-back task
(Moser et al. 2018) ⁹	37, 32%	BD I (37)	48, 42%	27.5 (8.1)	29.8 (8.5)	Not specified (n = 37)	MS (15), AP (30), AD (7)	Various stimuli n-back task
(Goikolea et al. 2019) ⁴⁵	31, 48%	BD (31)	31, 48%	30.5 (9.1)	31.1 (8.8)	Manic (n = 31)	MS (22), AP (31)	Letter n-back task
(Alonso-Lana et al. 2019) ⁴⁶	26, 42%	BD I (26)	26, 42%	39.2 (12.3)	40.2 (11.0)	Manic (baseline) (n = 26) Euthymic (follow-up) (n = 26)	MS (19), AP (22), AD (2)	Letter n-back task

NS = Not Specified, MS = Mood Stabilizers, AP = Antipsychotics, AD = Antidepressants.

eReferences

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