TECHNICAL COMMENTARY

Memory

Introduction

Memory involves encoding, storage and retrieval of information. Short-term memory is the ability to remember information after several seconds or minutes; and long-term memory is the ability to remember information over a longer duration. Working memory involves information being temporarily held as well as manipulated. Semantic memory is memory for general facts, episodic memory is memory for personal events, prospective memory is memory for future actions, and retrospective memory is memory for past events. Most memory tasks assess retrospective memory by measuring recall and recognition.

Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2010 that report results separately for people with a diagnosis of bipolar and related disorders. Reviews were identified by searching the databases MEDLINE, EMBASE, and PsycINFO. Hand searching reference lists of identified reviews was also conducted. When multiple copies of review topics were found, only the most recent and comprehensive review was included. Reviews with pooled data are prioritised for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis[1]. Reviews with less than 50% of items checked have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large or if there is a dose dependent response. We have also taken into account sample size and whether results are consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)[2]. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

Results

We found 14 systematic reviews that met our inclusion criteria[3-16].

- Moderate to high quality evidence shows medium-sized effects of poorer working and episodic memory in people with bipolar I disorder compared to controls. There were smaller effects of poorer working and episodic memory in people with bipolar II disorder compared to controls. Comparing people with bipolar I disorder directly with people with bipolar II disorder, small effects of poorer working memory and episodic memory in people with bipolar I disorder were found.

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Memory

- In people with either bipolar I or bipolar II disorder, there were medium-sized effects of poorer prospective and digit span memory compared to controls, with the effect for digit span backward being larger than for digit span forward.
- In people with first-episode bipolar disorder and youth with bipolar disorder (aged 13 years), there were small to medium-sized effects of poorer verbal, visual and working memory compared to controls. Compared to people with first-episode schizophrenia, people with first-episode bipolar disorder showed better verbal and working memory, with no differences in visual memory.
- In elderly people with bipolar disorder, moderate quality evidence found a medium-sized effect of poorer memory than in controls matched for age and years of education. Poor delayed recall was significant only during depression phases, while poor digit span was significant only during manic phases.
- Compared to people with major depression, moderate quality evidence found a medium-sized effect of poorer verbal memory in people with bipolar disorder during euthymia but not during a depressive phase.
- High quality evidence found small effects of poorer verbal and working memory with no differences in visual memory in people with bipolar disorder and a history of psychotic symptoms compared to people with bipolar disorder without a history of psychotic symptoms.
- High quality evidence found small effects of poorer verbal and visual memory in young first-degree relatives of people with bipolar disorder (aged 10 to 25 years) compared to controls. Compared to first-degree relatives of people with schizophrenia, moderate to high quality evidence found first-degree relatives of people with bipolar disorder had small to medium-sized effects of better verbal and working memory, with no differences in visual memory.
- High quality evidence suggests a small association between poorer memory and poorer general functioning.
- Moderate quality evidence suggests no changes in memory over time (~4-5 years) in people with bipolar disorder.

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Bo Q, Mao Z, Li X, Wang Z, Wang C, Ma X

Use of the MATRICS consensus cognitive battery (MCCB) to evaluate cognitive deficits in bipolar disorder: A systematic review and meta-analysis

PLoS ONE 2017; 12 (4); doi.org/10.1371/journal.pone.0176212

View review abstract online

Comparison	**Working memory in people with bipolar disorder vs. controls.**
Summary of evidence	**High quality evidence (large sample, consistent, precise, direct) suggests a medium-sized effect of poorer working memory in people with bipolar disorder.**
Working memory	
A significant, medium-sized effect of poorer working memory in people with bipolar disorder; 7 studies, N = 487, d = -0.62, 95%CI -0.74 to -0.49, $p < 0.05$, $I^2 = 0\%$, $p = 0.56$	
Consistency in results‡	Consistent
Precision in results§	Precise
Directness of results‖	Direct

Bora E, Pantelis C

Meta-analysis of Cognitive Impairment in First-Episode Bipolar Disorder: Comparison With First-Episode Schizophrenia and Healthy Controls

Schizophrenia Bulletin 2015; 41(5): 1095-1104

View review abstract online

Comparison 1	**Memory in people with first-episode bipolar disorder vs. controls.**
Summary of evidence	**Moderate to high quality evidence (medium to large sample, some inconsistency, precise, direct) suggests small to medium-sized effects of poorer verbal, visual and working memory in people with first-episode bipolar disorder.**

Memory	
Significant, small to medium-sized effects of poorer verbal memory, working memory, and visual memory in people with first-episode bipolar disorder; Verbal memory: 6 studies, N = 1,097, *d* = 0.63, 95%CI 0.39 to 0.86, *p* < 0.001, I^2 = 62%, *p* = 0.02 Visual memory: 5 studies, N = 590, *d* = 0.51, 95%CI 0.16 to 0.86, *p* = 0.004, I^2 = 68%, *p* = 0.01 Working memory: 9 studies, N = 10,140, *d* = 0.34, 95%CI 0.20 to 0.47, *p* < 0.001, I^2 = 0.6%, *p* = 0.42 Spatial working memory: 3 studies, N = 271, *d* = 0.38, 95%CI 0.06 to 0.71, *p* = 0.02, I^2 not reported Authors report no evidence of publication bias.	
Consistency in results	Consistent for working memory only.
Precision in results	Precise
Directness of results	Direct
Comparison 2	**Memory in people with first-episode bipolar disorder vs. people with first-episode schizophrenia.**
Summary of evidence	**Moderate to high quality evidence (medium to large samples, consistent, precise, direct) shows a medium-sized effect of poorer verbal memory in people with first-episode schizophrenia. Moderate quality evidence (inconsistent) also shows a small to medium-sized effect of poorer working memory, with no differences in visual memory.**
Memory	
Significant, small to medium-sized effects of poorer verbal memory, working memory and verbal working memory in people with first-episode schizophrenia compared with first-episode bipolar disorder; All verbal memory tasks: 7 studies, N = 832, *d* = 0.47, 95%CI 0.28 to 0.65, *p* < 0.001, I^2 = 39.5%, *p* = 0.13 Working memory: 8 studies, N = 774, *d* = 0.35, 95%CI 0.11 to 0.59, *p* = 0.005, I^2 = 59.2%, *p* = 0.02 Verbal working memory: 8 studies, N = 774, *d* = 0.33, 95%CI 0.08 to 0.57, *p* = 0.009, I^2 not reported *No significant differences in;* Digit span forwards: 4 studies, N = 435, *d* = 0.18, 95%CI -0.03 to 0.38, *p* = 0.09, I^2 not reported Digit span backwards: 6 studies, N = 536, *d* = 0.13, 95%CI -0.04 to 0.31, *p* = 0.14, I^2 not reported Visual memory: 4 studies, N = 406, *d* = 0.28, 95%CI -0.05 to 0.60, *p* = 0.09, I^2 = 66.2%, *p* = 0.05 Authors report no publication bias. Meta-regression analysis revealed between-group differences in working memory were more	

significant in studies that included younger people with first-episode schizophrenia. No differences were found for males vs. females.	
Consistency in results	Consistent for verbal memory, inconsistent for working memory and visual memory.
Precision in results	Precise
Directness of results	Direct

Bora E, Ozerdem A

A meta-analysis of neurocognition in youth with familial high risk for bipolar disorder

European Psychiatry 2017; 44: 17-23

View review abstract online

Comparison	**Memory in first-degree relatives aged 10 to 25 years of a person with bipolar disorder vs. controls.**
Summary of evidence	**High quality evidence (large sample, consistent, precise, direct) suggests small effects of poorer verbal and visual memory, with no significant differences in working memory in young relatives.**
Memory	
Small effects of poorer verbal and visual memory in relatives; Verbal memory: 7 studies, N = 841, d = 0.21, 95%CI 0.05 to 0.37, p = 0.01, I^2 = 25%, p = 0.24 Visual memory: 4 studies, N = 404, d = 0.35, 95%CI 0.12 to 0.58, p = 0.003, I^2 = 25%, p = 0.26 *There were no significant differences in working memory;* 8 studies, N = 870, d = 0.13, 95%CI -0.04 to 0.29, p = 0.12, I^2 = 29%, p = 0.20	
Consistency	Consistent
Precision	Precise
Directness	Direct

Bora E

A comparative meta-analysis of neurocognition in first-degree relatives of patients with schizophrenia and bipolar disorder

European Psychiatry 2017; 45: 121-8

View review abstract online

Comparison 1	**Memory in first-degree relatives of people with bipolar disorder vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large samples, some inconsistencies, precise, direct) suggests no differences in verbal, visual memory and working memory.**
Memory	
There were no significant differences in; Verbal memory: 7 studies, N = 603, d = 0.10, 95%CI -0.10 to 0.31, p = 0.32, I^2 = 33%, p = 0.18 Visual memory: 4 studies, N = 457, d = 0.30, 95%CI -0.16 to 0.77, p = 0.20, I^2 = 81%, p < 0.001 Working memory: 9 studies, N = 781, d = 0.12, 95%CI -0.13 to 0.37, p = 0.34, I^2 = 64%, p = 0.005 There was no evidence of publication bias.	
Consistency	Consistent for verbal memory, inconsistent for visual memory.
Precision	Precise
Directness	Direct
Comparison 2	**Memory in first-degree relatives of people with bipolar disorder vs. first-degree relatives of people with schizophrenia.**
Summary of evidence	**Moderate to high quality evidence (large samples, inconsistent, precise, direct) suggests small to medium-sized effects of better verbal and working memory in first-degree relatives of people with bipolar disorder, with no differences in visual memory.**
Memory	
Significant, small to medium-sized effects of better working and verbal memory in relatives of bipolar patients; Working memory: 10 studies, N = 589, d = 0.42, 95%CI 0.18 to 0.66, p < 0.001, I^2 = 59%, p = 0.009 Verbal memory: 8 studies, N = 815, d = 0.28, 95%CI 0.04 to 0.53, p = 0.02, I^2 = 49%, p = 0.06 *No significant differences in;*	

Delayed recall: 7 studies, N = 761, *d* = 0.29, 95%CI -0.02 to 0.59, *p* = 0.06, I^2 = 62%, *p* = 0.02 Visual memory: 4 studies, N = 347, *d* = 0.35, 95%CI -0.10 to 0.79, *p* = 0.13, I^2 = 74%, *p* = 0.008 Younger age in the relatives of people with schizophrenia was associated with greater between-group differences in working memory.	
Consistency	Inconsistent
Precision	Precise
Directness	Direct

Bora E

Neurocognitive features in clinical subgroups of bipolar disorder: A meta-analysis

Journal of Affective Disorders 2018; 229: 125-34

View review abstract online

Comparison 1	**Memory in people with bipolar I disorder vs. people with bipolar II disorder.**
Summary of evidence	**High quality evidence (large sample, consistent, precise, direct) suggests a small effect of poorer verbal memory in people with bipolar I disorder, with no differences on working or visual memory (moderate to high quality; inconsistent).**
Memory	
Small, significant effect of poorer verbal memory in people with bipolar I disorder; Verbal memory: 15 studies, N = 1,459, *d* = 0.26, 95%CI 0.11 to 0.41, *p* < 0.001, I^2 = 38%, *p* = 0.07 *There were no significant differences in;* Working memory: 12 studies, N = 1,106, *d* = 0.02, 95%CI -0.13 to 0.17, *p* = 0.29, I^2 = 27%, *p* = 0.18 Visual memory: 13 studies, N = 967, *d* = 0.15, 95%CI -0.10 to 0.41, *p* = 0.23, I^2 = 70%, *p* = 0.001	
Consistency in results	Consistent, apart from visual memory.
Precision in results	Precise
Directness of results	Direct
Comparison 2	**Memory in people with bipolar disorder and a history of psychotic symptoms vs. people with bipolar disorder and no**

	history of psychotic symptoms.
Summary of evidence	**High quality evidence (large samples, consistent, precise, direct) suggests small effects of poorer verbal and working memory in people with bipolar disorder and a history of psychotic symptoms, with no differences in visual memory.**
Memory	
Small, significant effects of greater verbal and working memory impairment in people with a history of psychosis; Verbal memory: 13 studies, N = 1,183, d = 0.28, 95%CI 0.16 to 0.40, $p < 0.001$, I^2 = 4%, p = 0.41 Working memory: 15 studies, N = 1,337, d = 0.13, 95%CI 0.02 to 0.24, p = 0.02, I^2 = 0%, p = 0.79 *There were no significant differences in;* Visual memory: 6 studies, N = 509, d = -0.02, 95%CI -0.19 to 0.16, p = 0.87, I^2 = 0%, p = 0.89 There were no significant differences in effect sizes between euthymic and non-euthymic or bipolar I and II disorder samples.	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Bora E, McIntyre RS, Ozerdem A

Neurococognitive and neuroimaging correlates of obesity and components of metabolic syndrome in bipolar disorder: a systematic review

Psychological medicine 2019; 49: 738-49

View review abstract online

Comparison	**Memory in overweight people with bipolar disorder vs. normal weight people with bipolar disorder.**
Summary of evidence	**Moderate quality evidence (small to medium-sized samples, some inconsistency, precise, direct) shows no differences in memory.**
Memory	

No significant differences between groups on; Verbal memory: 5 studies, N = 330, *d* = 0.21, 95%CI -0.16 to 0.51, *p* = 0.27, I^2 = 59%, *p* = 0.04 Visual memory: 3 studies, N = 163, *d* = 0.25, 95%CI -0.08 to 0.57, *p* = 0.14, I^2 = 0%, *p* = 0.51 Working memory: 3 studies, N = 163, *d* = 0.27, 95%CI -0.05 to 0.60, *p* = 0.10, I^2 = 0%, *p* = 0.64

Consistency in results	Consistent, apart from verbal memory.
Precision in results	Precise
Directness of results	Direct

Bourne C, Aydemir O, Balanza-Martinez V, Bora E, Brissos S, Cavanagh JT, Clark L, Cubukcuoglu Z, Dias VV, Dittmann S, Ferrier IN, Fleck DE, Frangou S, Gallagher P, Jones L, Kieseppa T, Martinez-Aran A, Melle I, Moore PB, Mur M, Pfennig A, Raust A, Senturk V, Simonsen C, Smith DJ, Bio DS, Soeiro-de-Souza MG, Stoddart SD, Sundet K, Szoke A, Thompson JM, Torrent C, Zalla T, Craddock N, Andreassen OA, Leboyer M, Vieta E, Bauer M, Worhunsky PD, Tzagarakis C, Rogers RD, Geddes JR, Goodwin GM

Neuropsychological testing of cognitive impairment in euthymic bipolar disorder: an individual patient data meta-analysis

Acta Psychiatrica Scandinavica 2013; 128: 149-62

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Comparison	**Memory in people with bipolar disorder vs. controls, adjusted for age, IQ and gender.**
Summary of evidence	**Moderate to high quality evidence (large sample, inconsistent, precise, direct) suggests small to medium-sized effects of poorer digit span memory in people with bipolar disorder compared to controls. The effect for digit span backward was larger than for digit span forward.**

Memory
Small to medium-sized, significant effects of poor digit span memory in euthymic bipolar disorder; Digit span forward: N = 1,183, ES = 0.30, 95%CI 0.20 to 0.40, *p* < 0.001, I^2 = 71% Digit span backward: N = 1,183, ES = 0.60, 95%CI 0.51 to 0.69, *p* < 0.001, I^2 = 84%

Consistency in results	Inconsistent

Precision in results	Precise
Directness of results	Direct

Cotrena C, Damiani Branco L, Ponsoni A, Samame C, Milman Shansis F, Paz Fonseca R

Executive functions and memory in bipolar disorders I and II: new insights from meta-analytic results

Acta Psychiatrica Scandinavica 2020; 141: 110-30

View review abstract online

Comparison 1	**Memory in people with bipolar I disorder vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large samples, inconsistent, precise, direct) shows medium-sized effects of poorer working and episodic memory in people with bipolar I disorder.**
Memory	
Small to medium-sized effects showed people with bipolar I disorder were more impaired on; Working memory: 64 studies, N = 4,294, g = 0.55, 95%CI 0.46 to 0.64, $p < 0.05$, I^2 = 64%, $p < 0.001$ Episodic memory: 67 studies, N = 7,931, g = 0.59, 95%CI 0.50 to 0.68, $p < 0.05$, I^2 = 73%, $p <$ 0.0001	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct
Comparison 2	**Memory in people with bipolar II disorder vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large samples, inconsistent, precise, direct) shows small to medium-sized effects of poorer working and episodic memory in people with bipolar II disorder.**
Memory	
Small to medium-sized effects showed people with bipolar II disorder were more impaired on; Working memory: 14 studies, N = 1,460, g = 0.42, 95%CI 0.27 to 0.57, $p < 0.05$, I^2 = 45%, p = 0.04 Episodic memory: 13 studies, N = 1,266, g = 0.33, 95%CI 0.19 to 0.46, $p < 0.05$, I^2 = 43%, p = 0.05	

Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct
Comparison 3	**Memory in people with bipolar I disorder vs. people with bipolar II disorder.**
Summary of evidence	**Moderate to high quality evidence (large samples, some inconsistency, precise, direct) shows small effects of poorer working and episodic memory in people with bipolar I disorder.**
Memory	
Small effects showed people with bipolar I disorder were more impaired than people with bipolar II disorder on; Working memory: 8 studies, N = 857, *g* = 0.22, 95%CI 0.08 to 0.35, *p* < 0.05, I^2 = 13%%, *p* = 0.33 Episodic memory: 8 studies, N = 743, *g* = 0.35, 95%CI 0.15 to 0.55, *p* < 0.05, I^2 = 60%, *p* = 0.01 Immediate verbal episodic memory: 7 studies, N = 520, *g* = 0.32, 95%CI 0.10 to 0.54, *p* < 0.05, I^2 = 45%, *p* = 0.09 Delayed verbal episodic memory: 6 studies, N = 486, *g* = 0.30, 95%CI 0.02 to 0.57, *p* < 0.05, I^2 = 66%, *p* = 0.01 Visual episodic memory: 5 studies, N = 536, *g* = 0.31, 95%CI 0.05 to 0.57, *p* < 0.05, I^2 = 59%, *p* = 0.05 *There were no significant differences on;* Digit span forward: 5 studies, N = 634, *g* = 0.11 95%CI -0.06 to 0.27, I^2 = 0%, *p* = 0.56	
Consistency in results	Inconsistent, apart from inhibition.
Precision in results	Precise
Directness of results	Direct

Depp CA, Mausbach BT, Harmell AL, Savla GN, Bowie CR, Harvey PD, Patterson TL

Meta-analysis of the association between cognitive abilities and everyday functioning in bipolar disorder

Bipolar Disorders 2012; 14: 217-26

View review abstract online	
Comparison	**Associations between memory and functioning in people with bipolar disorder.**
Summary of evidence	**High quality evidence (large sample, consistent, precise, direct) suggests a small association between poorer memory and poorer general functioning.**
Memory	
Significant, small associations between poor learning and memory and working memory and poor general functioning; Verbal learning and memory: 17 studies, N = 895, *r* = 0.23, 95%CI 0.14 to 0.31, *p* < 0.0045, Q*p* = 0.088 Visual learning and memory: 5 studies, N = 381, *r* = 0.26, 95%CI 0.16 to 0.35, *p* < 0.0045, Q*p* = 0.597 Working memory: 9 studies, *r* = 0.29, 95%CI 0.20 to 0.38, *p* < 0.0045, Q*p* = 0.177	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Elias LR, Miskowiak KW, Vale AM, Kohler CA, Kjaerstad HL, Stubbs B, Kessing LV, Vieta E, Maes M, Goldstein BI, Carvalho AF

Cognitive Impairment in Euthymic Pediatric Bipolar Disorder: A Systematic Review and Meta-Analysis

Journal of the American Academy of Child & Adolescent Psychiatry 2017; 56: 286-96

View review abstract online

Comparison	**Memory in euthymic youth with bipolar disorder vs. controls of similar age (mean 13 years) and IQ (mean 104).**
Summary of evidence	**Moderate to high quality evidence (medium to large samples, some inconsistency, precise, direct) suggests large, significant effects of poorer verbal, visual and working memory in euthymic youth with bipolar disorder.**
Memory	

Large, significant effect of poorer verbal, visual and working memory in euthymic youth with bipolar disorder; Visual learning and memory: 4 studies, N = 135, g = 0.78, 95%CI 0.43 to 1.13, $p < 0.001$, I^2 = 0%, $p > 0.05$ Verbal learning and memory: 7 studies, N = 401, g = 0.76, 95%CI 0.29 to 1.22, p = .001, I^2 = 76%, $p < 0.05$ Working memory: 8 studies, N = 433, g = 0.99, 95%CI 0.64 to 1.35, $p < 0.001$, I^2 = 62%, $p < 0.05$

Consistency in results	Consistent for visual learning and memory, inconsistent for verbal learning and memory and working memory.
Precision in results	Precise
Directness of results	Direct

Samame C, Martino DJ, Strejilevich SA

A quantitative review of neurocognition in euthymic late-life bipolar disorder

Bipolar Disorders 2013; 15: 633-44

View review abstract online

Comparison	**Memory in older people with bipolar disorder vs. controls matched for age and years of education.**
Summary of evidence	**Moderate quality evidence (medium-sized samples, some consistency, precise, direct) suggests a medium-sized effect of poorer memory in elderly people with bipolar disorder. Poor delayed recall was associated with depression symptoms, while poor digit span was associated with manic symptoms.**

Memory
Medium-sized, significant effects of poorer memory in elderly people with bipolar disorder; Delayed recall: 5 studies, N = 415, g = 0.71, 95%CI 0.33 to 1.08, $p < 0.001$, I^2 = 64%, p = 0.02 Digit span forwards: 3 studies, N = 301, g = 0.61, 95%CI 0.38 to 0.85, $p < 0.001$, I^2 = 0%, p = 0.95 Subgroup analyses showed no changes in the effect sizes according to age or years of education. When the analysis included only studies of patients in a depression phase, only delayed recall showed an effect (g = 0.37). When the analysis included only studies of patients in a manic phase, only digit span showed a significant effect (g = 0.48).

Consistency in results	Inconsistent for delayed recall, consistent for digit span.
Precision in results	Precise
Directness of results	Direct

Samame C, Martino DJ, Strejilevich SA

Longitudinal course of cognitive deficits in bipolar disorder: a meta-analytic study

Journal of Affective Disorders 2014; 164: 130-8

View review abstract online

Comparison	**Changes in memory over time in people with bipolar disorder.**
Summary of evidence	**Moderate quality evidence (small samples, consistent, precise, direct) suggests no changes in memory over time (~4-5 years).**
Memory	
There were no significant changes over time; Delayed list recall: 4 studies, N = 154, follow up = 5.06 years, *d* = 0.04, 95%CI -0.18 to 0.27, *p* = 0.71, I^2 = 0%, *p* = 0.53 Backward digit span: 4 studies, N = 181, follow up = 4.10 years, *d* = -0.08, 95%CI -0.28 to 0.11, *p* = 0.41, I^2 = 0%, *p* = 0.92 Forward digit span: 3 studies, N = 138, follow up = 5.06 years, *d* = 0.22, 95%CI 0.00 to 0.44, *p* = 0.05, I^2 = 0%, *p* = 0.52	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Samame C, Szmulewicz AG, Valerio MP, Martino DJ, Strejilevich SA

Are major depression and bipolar disorder neuropsychologically distinct? A meta-analysis of comparative studies

European Psychiatry 2017; 39: 17-26 View review abstract online	
Comparison	**Memory in people with bipolar disorder vs. people with major depression.**
Summary of evidence	**Moderate quality evidence (small samples, consistent, precise, direct) suggests a medium-sized effect of better verbal memory in people with major depression compared to people with bipolar disorder who are in a euthymic phase. There were no differences during a depression phase.**
Memory	
A medium-sized significant effect of better verbal memory (list learning) in people with major depressive disorder compared to people with bipolar disorder during euthymia only; 3 studies, N = 149, g = 0.65, 95%CI 0.31 to 0.98, $p < 0.001$, I^2 = 0%, p = 0.45 *There were no differences between groups on verbal memory (list learning) during depression;* 4 studies, N = 151, g = 0.15, 95%CI -0.28 to 0.58, p = 0.50, I^2 = 45%, p = 0.14	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Zhou FC, Wang YY, Zheng W, Ungvari GS, Ng CH, Yuan Z, Xiang, YT

Prospective memory in bipolar disorder: A meta-analysis

Psychiatry Research 2018; 259: 184-90
View review abstract online

Comparison	**Prospective memory in people with bipolar disorder vs. controls.**
Summary of evidence	**Moderate to high quality evidence (medium-sized samples, consistent, precise, direct) suggests medium-sized effects of poorer event-based and time-based prospective memory in people with bipolar disorder.**
Prospective memory	

Memory

Medium-sized, significant effects of poorer prospective memory in people with bipolar disorder; Event-based: 4 studies, N = 367, SMD = -0.51, 95%CI -0.78 to -0.23, p = 0.0003, I^2 = 37%, p = 0.15 Time-based: 4 studies, N = 367, SMD = -0.82, 95%CI -1.11 to -0.52, p < 0.0001, I^2 = 41%, p = 0.17	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Explanation of acronyms

CI = confidence interval, *d* = Cohen's d, ES = effect size, *g* = Hedges's g, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error, N = number of participants, *p* = probability of rejecting a null hypothesis of no differences between groups, Q = test for heterogeneity, , *r* = correlation coefficient , SMD = standardised mean difference

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Explanation of technical terms

* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias – selective reporting of results; publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small[17].

† Different effect measures are reported by different reviews.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. Less than 0.4 represents a small effect, around 0.5 a medium effect, and over 0.8 represents a large effect[17].

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or < 0.2[18]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

Correlation coefficients (eg, r) indicate the strength of association or relationship

between variables. They can provide an indirect indication of prediction, but do not confirm causality due to possible and often unforseen confounding variables. An r of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised (*b*) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent considerable heterogeneity and over this is considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula[17];

$$I^2 = \left(\frac{Q - df}{Q}\right) \times 100\%$$

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, these criteria should be relaxed[19].

‖ Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and/or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available and is therefore inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.

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