TECHNICAL COMMENTARY

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BIPOLAR DISORDERS LIBRARY

Cognition in bipolar disorder vs. schizophrenia

Introduction

Bipolar disorder is characterised by intermittent periods of mania and depression. Mania involves elevated or irritable mood, which is often accompanied by inflated self-esteem or grandiosity, decreased need for sleep, distractibility, psychomotor agitation, or excessive involvement in pleasurable activities. Manic episodes may involve psychotic symptoms such as grandiose delusions. Depressive episodes may be characterised by extended periods of sadness, a loss of interest in activities, loss of appetite, decreased energy, feelings of worthlessness, difficulty concentrating and suicidal ideation. Bipolar I disorder is mostly characterised by manic symptoms whereas Bipolar II disorder is mostly characterised by depressive episodes.

Schizophrenia is characterised by positive, negative, and disorganised symptoms. Positive symptoms refer to experiences additional to what would be considered normal experience, such as hallucinations and delusions. Negative symptoms feature an absence of normal function, and may include blunted affect, impoverished thinking, alogia, asociality, avolition and anhedonia. Alogia is often manifested as poverty of speech; asociality involves reduced social interaction; avolition refers to poor hygiene and reduced motivation; and anhedonia is defined as an inability to experience pleasure. Disorganised symptoms include disorganised thought and speech. Depressive symptoms are also common, with many individuals experiencing depression after a psychotic episode.

Neurocognitive deficits are a core feature of both schizophrenia and bipolar disorder. People with either disorder may perform poorly on cognitive tasks assessing intelligence, memory, executive functioning, language, information processing and attention. Establishing differences in these cognitive domains may assist correct diagnosis and treatment of the two disorders.

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

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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 seven systematic reviews that met our inclusion criteria[3-9].

- Moderate to high quality evidence finds large effects of poorer overall cognition, attention, and social cognition in people with schizophrenia compared to people with bipolar disorder. There were also medium-sized effects of poorer speed of processing, working memory, learning, reasoning, and problem solving in people with schizophrenia.
- High quality evidence found a small effect of poorer overall cognition in people with schizoaffective disorder (particularly depressive type) compared to people with bipolar disorder, regardless of cognitive domain, bipolar type (I or I and II mixed), age, sex, duration of illness, antipsychotic use, or symptom severity.
- Moderate to high quality evidence shows a medium-sized effect of poorer premorbid IQ in people with first-episode schizophrenia compared to people with first-episode bipolar disorder. Moderate to low quality evidence also shows a medium-sized effect of poorer current IQ in people with first-episode schizophrenia.
- Moderate to high quality evidence shows medium-sized effects of poorer verbal memory and verbal fluency in people with first-episode schizophrenia compared to people with first-episode bipolar disorder. Moderate quality evidence also shows small effects of poorer working memory and processing speed in people with first-episode schizophrenia, with no differences in visual memory.
- Moderate to high quality evidence finds a small effect of poorer pre-onset cognitive functioning, and a medium-sized effect of poorer post-onset cognitive functioning, in people with bipolar disorder compared to controls. In people with schizophrenia compared to controls, there was a medium-sized effect of poorer pre-onset cognitive functioning and a large effect of poorer post-onset cognitive functioning.
- In children with schizophrenia (mean age ~15 years) compared to age-matched controls, high quality evidence found large effects of poor attention, working memory, verbal fluency, verbal learning and memory and visual memory in early onset schizophrenia. Moderate to high quality evidence also found large effects of poor general cognitive ability, visuospatial ability, processing speed, executive control, and a medium-sized effect of poor motor skills in early onset schizophrenia. In children with bipolar disorder (mean age ~13 years) compared to age-matched controls, high quality evidence found a large effect of poor processing speed, and medium-sized effects of poor attention, executive control, working memory, verbal fluency, verbal learning and memory, visuospatial ability, and visual memory. Moderate to high quality evidence also found a medium-sized effect of poor general cognitive ability in paediatric bipolar disorder.

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- Moderate quality evidence suggests similar, medium to large effects of poor semantic inhibition in people with bipolar disorder and in people with schizophrenia when compared to controls.
- Moderate to high quality evidence finds a medium-sized effect of poorer social cognition in people with schizophrenia than in people with bipolar disorder on Theory of Mind and negative facial emotion recognition tasks, particularly in male patients. There were no differences on positive (happy) facial emotion recognition tasks.

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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	**Cognitive functioning in people with first-episode bipolar disorder vs. people with first-episode schizophrenia.**
Summary of evidence	***Memory:*** **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 compared to people with first-episode bipolar disorder. Moderate quality evidence (inconsistent) also shows a small effect of poorer working memory. There were no significant differences in digit span or visual memory.** ***Verbal fluency:*** **Moderate to high quality evidence (medium to large samples, consistent, precise, direct) shows a medium-sized effect of poorer verbal fluency in people with first-episode schizophrenia compared to people with first-episode bipolar disorder.** ***Processing speed:*** **Moderate quality evidence (medium to large samples, inconsistent) shows a small effect of poorer processing speed in people with first-episode schizophrenia compared to people with first-episode bipolar disorder.** ***IQ:*** **Moderate to high quality evidence (medium to large samples, consistent, precise, direct) shows a medium-sized effect of poorer premorbid IQ in people with first-episode schizophrenia compared to people with first-episode bipolar disorder. Moderate to low quality evidence (imprecise and inconsistent) also shows a medium-sized effect of poorer current IQ in people with first-episode schizophrenia.** ***Global cognition:*** **Moderate to high quality evidence (large sample, inconsistent, precise, direct) shows a small effect of poorer global cognition in people with first-episode schizophrenia compared to people**

	with first-episode bipolar disorder. **No differences in attention or reasoning are reported.**
Global cognition	
A significant, small effect of poorer global cognition in people with first-episode schizophrenia compared with first-episode bipolar disorder; 14 studies, N = 1,427, *d* = 0.28, 95%CI 0.12 to 0.44, *p* < 0.001, I^2 = 48.8%, *p* = 0.02 Authors report no publication bias. No differences were found for males vs. females or younger vs. older patients.	
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.	
Processing speed	
Significant, small to medium-sized effects of poorer processing speed in people with first-episode schizophrenia compared with first-episode bipolar disorder; All speed tasks: 6 studies, N = 679, *d* = 0.33, 95%CI 0.08 to 0.59, *p* = 0.009, I^2 = 58.9%, *p* = 0.03 TMT A: 3 studies, N = 328, *d* = 0.45, 95%CI 0.23 to 0.68, *p* < 0.001 TMT B: 3 studies, N = 328, *d* = 0.47, 95%CI 0.14 to 0.80, *p* = 0.006 Digit symbol: 3 studies, N = 450, *d* = 0.71, 95%CI 0.36 to 1.06, *p* < 0.001 Authors report no publication bias. No differences were found for males vs. females or younger vs. older patients.	

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IQ	
Significant, medium-sized effects of lower premorbid and current IQ in people with first-episode schizophrenia compared with first-episode bipolar disorder; Premorbid IQ: 7 studies, N = 728, d = 0.50, 95%CI 0.30 to 0.69, $p < 0.001$, I^2 = 36.8%, p = 0.15 Current IQ: 6 studies, N = 533, d = 0.63, 95%CI 0.36 to 0.91, $p < 0.001$, I^2 = 67.9%, p = 0.05 Authors report no publication bias. No differences were found for males vs. females or younger vs. older patients.	
Fluency	
Significant, medium-sized effects of poorer fluency in people with first-episode schizophrenia compared with first-episode bipolar disorder; All fluency tasks: 7 studies, N = 865, d = 0.50, 95%CI 0.33 to 0.66, $p < 0.001$, I^2 = 22.0%, p = 0.26 Letter: 5 studies, N = 542, d = 0.42, 95%CI 0.24 to 0.60, $p < 0.001$ Category: 3 studies, N = 328, d = 0.77, 95%CI 0.0 to 1.53, p = 0.05 Authors report no publication bias. No differences were found for males vs. females or younger vs. older patients.	
Attention	
No significant differences in attention; 2 studies, N = 101, d = 0.05, 95%CI −0.38 to 0.47, p = 0.83, I^2 = 0%, p = 0.62 Authors report no publication bias. No differences were found for males vs. females or younger vs. older patients.	
Reasoning	
No significant differences in reasoning; 2 studies, N = 218, d = 0.23, 95%CI −0.09 to 0.56, p = 0.16, I^2 = 26.3%, p = 0.24 Authors report no publication bias. No differences were found for males vs. females or younger vs. older patients.	
Consistency in results‡	Consistent for verbal memory, premorbid IQ, fluency, attention and reasoning. Inconsistent for global cognition, working memory, visual memory, psychomotor speed, and current IQ.
Precision in results§	Precise for global cognition, verbal memory, working memory, visual memory, digit span, psychomotor tasks, TMT A, premorbid IQ, and

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	fluency (all and letter). Imprecise for TMT B, digit symbol, current IQ, category fluency, attention, and reasoning.
Directness of results‖	Direct

Bora E, Pantelis C

Social cognition in schizophrenia in comparison to bipolar disorder: A meta-analysis

Schizophrenia Research 2016; 175: 72-8

View review abstract online

Comparison	**Social cognition in people with bipolar disorder vs. people with schizophrenia.**
Summary of evidence	**Moderate to high quality evidence (large samples, inconsistent, precise, direct) suggests a medium-sized effect of poorer social cognition in people with schizophrenia than in people with bipolar disorder on Theory of Mind and negative facial emotion recognition tasks, particularly for male patients. There were no differences on positive (happy) facial emotion recognition tasks.**

Social cognition

A significant, medium-sized effect of poorer social cognition in people with schizophrenia;

Overall social cognition: 26 studies, N = 2,376, d = 0.45, 95%CI 0.31 to 0.60, $p < 0.001$, Q$p < 0.001$

The effect size was slightly smaller when the analysis included only samples of patients with bipolar disorder I (d = 0.39).

The effect size was larger for Theory of Mind tests than for facial emotion recognition tests (d = 0.57 vs. d = 0.39). The effect was significant only for negative, angry, and sad facial emotion recognition tests, and not happy facial emotion recognition tests.

Effect sizes were larger in studies that had a higher percentage of males in their schizophrenia sample.

There were no effects of diagnostic tool (DSM-IV/IV-TR vs. DSM-IIIR), study setting (acute vs. non-acute), age, negative or positive symptoms, and age of onset and duration of bipolar disorder.

Consistency in results	Inconsistent
Precision in results	Precise

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Directness of results	Direct

Li W, Zhou FC, Zhang L, Ng CH, Ungvari GS, Li J, Xiang YT

Comparison of cognitive dysfunction between schizophrenia and bipolar disorder patients: A meta-analysis of comparative studies

Journal of Affective Disorders 2020; 274: 652-61

View review abstract online

Comparison	**Cognitive functioning in people with bipolar disorder vs. people with schizophrenia.**
Summary of evidence	**Moderate to high quality evidence (mostly large samples, inconsistent, precise, direct) finds large effects of poorer overall cognition, attention, and social cognition in people with schizophrenia. There were medium-sized effects of poorer speed of processing, working memory, learning, reasoning, and problem solving.**

Overall cognition

A large effect size showed poorer overall cognition in people with schizophrenia;

3 studies, N = 209, SMD = -0.80, 95%CI -1.21 to -0.39, p = 0.0001, I^2 = 49%

Attention

A large effect size showed poorer attention in people with schizophrenia;

10 studies, N = 1,344, SMD = -2.56, 95%CI -3.55 to -1.57, p = 0.00001, I^2 = 97%

Meta-regression analyses found that studies with older samples reported smaller effect sizes.

Social cognition

A large effect size showed poorer social cognition in people with schizophrenia;

8 studies, N = 1,211, SMD = -0.86, 95%CI -1.13 to -0.58, p = 0.00001, I^2 = 70%

Speed of processing

A medium effect size showed slower speed of processing in people with schizophrenia;

6 studies, N = 448, SMD = -0.75, 95%CI -1.00 to -0.49, p = 0.00001, I^2 = 37%

Working memory
A medium effect size showed poorer working memory in people with schizophrenia; 6 studies, N = 448, SMD = -0.68, 95%CI -0.91 to -0.45, *p* = 0.00001, I^2 = 25%
Learning
Medium effect sizes showed poorer learning in people with schizophrenia; Verbal learning: 12 studies, N = 9,518, SMD = -0.78, 95%CI -0.95 to -0.61, *p* = 0.00001, I^2 = 64% Visual learning: 11 studies, N = 1,449, SMD = -0.65, 95%CI -0.83 to -0.48, *p* = 0.00001, I^2 = 47% Meta-regression analyses found that studies with older samples reported smaller effect sizes (verbal learning only). Studies published more recently reported larger effect sizes (verbal learning only).
Reasoning and problem solving
A medium effect size showed poorer reasoning and problem solving in people with schizophrenia; 11 studies, N = 9,413, SMD = -0.61, 95%CI -0.93 to -0.29, *p* = 0.0002, I^2 = 91% Meta-regression analyses found that studies with older samples reported smaller effect sizes. Studies published more recently reported larger effect sizes.

Consistency in results	Mostly inconsistent
Precision in results	Mostly precise
Directness of results	Direct

Lynham AJ, Cleaver SL, Jones IR, Walters JTR

A meta-analysis comparing cognitive function across the mood/psychosis diagnostic spectrum

Psychological medicine 2020; June: 1-9

View review abstract online

Comparison	**Cognitive functioning in people with bipolar disorder vs. people with schizoaffective disorder.**
Summary of evidence	**High quality evidence (large sample, consistent, precise, direct) found a small effect size showing people with schizoaffective disorder (particularly depressive type) had poorer overall**

	cognition than people with bipolar disorder regardless of cognitive domain, bipolar type (I or I and II mixed), age, sex, duration of illness, antipsychotic use, and symptom severity.
Overall cognition **Composite of learning, executive function, speed of processing, verbal fluency, and working memory**	
A small effect size showed people with schizoaffective disorder performed worse than people with bipolar disorder; 10 studies, N = 5,695, *g* = -0.30, 95%CI -0.41 to -0.20, *p* < 0.0001, Q*p* = 0.56 People with schizoaffective depressive type showed a small effect of poorer cognition than people with schizoaffective bipolar type (*g* = 0.25, *p* = 0.05). There were no moderating effects of cognitive domain, bipolar type (I or I and II mixed), age, sex, duration of illness, antipsychotic use, psychotic, depressive, negative, or manic symptom severity.	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Nieto R, Castellanos F

A Meta-Analysis of Neuropsychological Functioning in Patients with Early Onset Schizophrenia and Paediatric Bipolar Disorder

Journal of Clinical Child & Adolescent Psychology 2012; 40(2): 266-280

View review abstract online

Comparison	**Cognitive performance in patients with early onset schizophrenia (EOS: mean age 15.8 years) and in paediatric bipolar disorder (PBD: mean age 13.6 years) vs. age-matched controls.**
Summary of evidence	**EOS vs. controls:** **High quality evidence (consistent, precise, direct, large samples) finds large effects of poor attention, working memory, verbal fluency, verbal learning and memory and visual memory in EOS.** **Moderate to high quality evidence (imprecise or inconsistent) finds large effects of poor general cognitive ability, visuospatial ability, processing speed, executive control, and a medium-**

	sized effect of poor motor skills in EOS. **PBD vs. controls:** **High quality evidence finds a large effect of poor processing speed, and medium-sized effects of poor attention, executive control, working memory, verbal fluency, verbal learning and memory, visuospatial ability, and visual memory in PBD.** **Moderate to high quality evidence (inconsistent) finds a medium-sized effect of poor general cognitive ability in PBD.** **Low quality evidence (1 small study) is unable to determine any differences in motor skills between PBD and controls.** **EOS vs. PBD:** **Low quality evidence (indirect) is unable to determine the differences in cognition in EOS vs. PBD.**
Processing speed	
Large effect of poorer processing speed in EOS and PBD vs. controls, with EOS showing significantly larger effect than PBD; EOS: 8 studies, N = 624, *g* = -1.27, 95%CI -1.99 to -0.55, *p* < 0.005, Q = 0.05, *p* = 0.99 publication bias *p* = 0.54 PBD: 7 studies, N = 478, *g* = -0.79, 95%CI -1.23 to -0.35, *p* < 0.005, Q = 2.63, *p* = 0.85 publication bias *p* = 0.77 Processing speed was significantly lower in EOS vs. controls than PBD vs. controls (*p* < 0.001). Moderator analyses revealed significantly smaller effect sizes in studies with a lower percentage of patients taking medications in both diagnostic groups. In studies of PBD, there were smaller effect sizes in studies with higher rates of euthymia and lower rates of comorbid attention deficit hyperactivity disorder (ADHD). In studies of EOS, there were smaller effect sizes in studies with higher percentages of right-handed participants and higher percentages of stable patients.	
General cognitive ability	
Large effect in EOS and a medium effect in PBD of lower general cognitive ability vs. controls; EOS: 9 studies, N = 667, *g* = -1.15, 95%CI -1.51 to -0.79, *p* < 0.005, Q = 17.19, *p* = 0.03 publication bias *p* = 0.46 PBD: 6 studies, N = 358, *g* = -0.42, 95%CI -0.64 to -0.20, *p* < 0.005, Q = 22.75, *p* < 0.001 publication bias *p* = 0.33 General cognitive ability was significantly lower in EOS vs. controls than PBD vs. controls (*p* < 0.001).	

Moderator analyses revealed significantly smaller effect sizes in PBD studies with a lower rates of comorbid ADHD.
Attention
Large effect in EOS and a medium effect in PBD of poorer attention vs. controls; EOS: 11 studies, N = 758, *g* = -1.01, 95%CI -1.37 to -0.65, *p* < 0.005, Q = 9.17, *p* = 0.52 publication bias *p* = 0.15 PBD: 8 studies, N = 538, *g* = -0.62, 95%CI -0.93 to -0.31, *p* < 0.005, Q = 5.07 *p* = 0.65 publication bias *p* = 0.56 Attention was significantly lower in EOS vs. controls than PBD vs. controls (*p* < 0.001). Moderator analyses revealed significantly smaller effect sizes in PBD studies with a lower percentage of patients taking medications, and in EOS studies with a higher percentage of patients taking antipsychotics. In PBD studies, there were smaller effect sizes in studies with lower rates of comorbid ADHD.
Working memory
Large effect in EOS and a medium effect in PBD of poorer working memory vs. controls; EOS: 6 studies, N = 464, *g* = -0.99, 95%CI -1.33 to -0.65, *p* < 0.005, Q = 6.18, *p* = 0.29 publication bias *p* = 0.24 PBD: 7 studies, N = 525, *g* = -0.68, 95%CI -0.99 to -0.37, *p* < 0.005, Q = 9.04 *p* = 0.17 publication bias *p* = 0.49 Working memory was significantly lower in EOS vs. controls than PBD vs. controls (*p* < 0.001). Moderator analyses revealed significantly smaller effect sizes in PBD studies with a lower percentage of patients taking mood stabilizers, and in EOS studies with a higher percentage of patients taking antipsychotics. Smaller effect sizes were reported in studies with a lower percentage of patients with acute psychotic symptoms or a lower percentage of manic patients.
Visuospatial ability
Large effect in EOS and a medium effect in PBD of poorer visuospatial ability vs. controls; EOS: 7 studies, N = 540, *g* = -0.96, 95%CI -1.28 to -0.64, *p* < 0.005, Q = 14.69, *p* = 0.02 publication bias *p* = 0.92 PBD: 3 studies, N = 234, *g* = -0.44, 95%CI -0.79 to -0.09, *p* = 0.02, Q = 1.56 *p* = 0.46 publication bias *p* = 0.86 Visuospatial ability was significantly lower in EOS vs. controls than PBD vs. controls (*p* < 0.001). Moderator analyses revealed significantly smaller effect sizes in studies with a higher percentage of

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males in both diagnostic groups.
Executive control
Large effect in EOS and a medium effect in PBD of poorer executive control vs. controls; EOS: 11 studies, N = 758, *g* = -0.95, 95%CI -1.72 to -0.63, *p* < 0.005, Q = 13.54, *p* = 0.19 publication bias *p* = 0.38 PBD: 9 studies, N = 605, *g* = -0.66, 95%CI -0.97 to -0.35, *p* < 0.005, Q = 5.46 *p* = 0.71 publication bias *p* = 0.80 Executive control was significantly lower in EOS vs. PBD (*p* < 0.001). Moderator analyses revealed significantly smaller effect sizes in PBD studies with a lower percentage of patients taking medication, and in EOS studies with a higher percentage of patients taking antipsychotics. Smaller effect sizes were reported in studies with a lower percentage of patients with acute psychotic symptoms or a lower percentage of manic patients.
Verbal fluency
Large effect in EOS and a medium effect in PBD of poorer verbal fluency vs. controls; EOS: 8 studies, N = 628, *g* = -0.95, 95%CI -1.31 to -0.59, *p* < 0.005, Q = 5.05, *p* = 0.65 publication bias *p* = 0.35 PBD: 9 studies, N = 631, *g* = -0.54, 95%CI -0.89 to -0.19, *p* < 0.005, Q = 4.36 *p* = 0.82 publication bias *p* = 0.17 Verbal fluency was significantly lower in EOS vs. controls than PBD vs. controls (*p* < 0.001). No significant moderators.
Verbal learning and memory
Large effect of poorer verbal learning and memory in EOS and PBD vs. controls; EOS: 9 studies, N = 627, *g* = -0.86, 95%CI -1.15 to -0.57, *p* < 0.005, Q = 4.41, *p* = 0.82 publication bias *p* = 0.56 PBD: 9 studies, N = 631, *g* = -0.83, 95%CI -1.18 to -0.48, *p* < 0.005, Q = 11.26 *p* = 0.19 publication bias *p* = 0.32 No significant difference between EOS vs. controls and PBD vs. controls (*p* ≥ 0.05). Moderator analyses revealed significantly smaller effect sizes in studies with a lower percentage of males in both diagnostic groups.
Visual memory

Large effect in EOS and a medium effect in PBD of poorer visual memory vs. controls; EOS: 4 studies, N = 213, *g* = -0.82, 95%CI -1.32 to -0.32, *p* < 0.005, Q = 2.58, *p* = 0.46 publication bias *p* = 0.88 PBD: 5 studies, N = 283, *g* = -0.44, 95%CI -0.93 to -0.05, *p* = 0.03, Q = 4.36 *p* = 0.96 publication bias *p* = 0.12 Visual memory was significantly lower in EOS vs. controls than PBD vs. controls (*p* < 0.001). No significant moderators.	
Motor skills	
Medium effect in EOS and very small effect in PBD of poorer motor skills vs. controls; EOS: 4 studies, N = 242, *g* = -0.58, 95%CI -1.19 to 0.03, *p* = 0.04, Q = 0.07, *p* = 0.99 publication bias *p* = 0.35 PBD: 1 study, N = 84, *g* = -0.07, 95%CI -0.15 to 0.01, *p* = 0.04 Motor skills were significantly lower in EOS vs. controls than PBD vs. controls (*p* < 0.01). No significant moderators.	
Consistency	Consistent, apart from general cognitive ability (EOS and PBD) and visuospatial ability (EOS)
Precision	Precise, apart from processing speed (EOS), executive control (EOS) and motor skills (EOS)
Directness	Direct, apart from EOS vs. PBD

Trotta A, Murray RM, MacCabe JH

Do premorbid and post-onset cognitive functioning differ between schizophrenia and bipolar disorder? A systematic review and meta-analysis

Psychological Medicine 2015; 45: 381-94

View review abstract online

Comparison	**Pre- and post-illness onset cognitive functioning in people with bipolar disorder or schizophrenia vs. controls.**
Summary of evidence	**Moderate to high quality evidence (large samples, inconsistent, precise, direct) finds a small effect of poorer pre-onset cognitive functioning and a medium-sized effect of poorer post-onset**

	cognitive functioning in people with bipolar disorder. In people with schizophrenia, there was a medium-sized effect of poorer pre-onset cognitive functioning and a large effect of poorer post-onset cognitive functioning.
Pre-onset cognitive functioning	
Significant, medium-sized effect of poorer pre-onset cognitive functioning in people with schizophrenia than controls; 17 studies, N = 774,131, SMD = -0.597, 95%CI -0.707 to -0.487, $p < 0.0001$, $I^2 = 72\%$, $p < 0.0001$ Subgroup analysis found a smaller effect in prospective than retrospective studies (-0.406 vs. -0.675). *Significant, small effect of poorer pre-onset cognitive functioning in people with bipolar disorder than controls;* 17 studies, N = 773,408, SMD = -0.113, 95%CI -0.202 to -0.024, $p = 0.013$, $I^2 = 34\%$, $p = 0.06$ Subgroup analysis found a smaller effect in prospective than retrospective studies (-0.029 vs. -0.147). There were no moderating effects of medications, age at time of assessment, duration of illness, clinical status, source population, year of publication and cognitive test used.	
Post-onset cognitive functioning	
Significant, large effect of poorer post-onset cognitive functioning in people with schizophrenia than controls; 17 studies, N = 2,487, SMD = -1.369, 95%CI -1.578 to -1.160, $p < 0.0001$, $I^2 = 78\%$, $p < 0.0001$ Subgroup analysis found a smaller effect in patients during their first episode of psychosis than those not in their first episode of psychosis (-1.111 vs. -1.432). *Significant, medium-sized effect of poorer pre-onset cognitive functioning in people with bipolar disorder than controls;* 17 studies, N = 2,211, SMD = -0.623, 95%CI -0.717 to -0.529, $p < 0.0001$, $I^2 = 82\%$, $p < 0.0001$ Subgroup analysis found a smaller effect in patients during their first episode of psychosis than those not in their first episode of psychosis (-0.277 vs. -0.691). Potential effect modifiers There were no moderating effects of medications, age at time of assessment, duration of illness, clinical status, source population, year of publication and cognitive test used.	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

Wang K, Song LL, Cheung EFC, Lui SSY, Shum DHK, Chan RCK

Bipolar disorder and schizophrenia share a similar deficit in semantic inhibition: A meta-analysis based on hayling sentence completion test performance

Progress in Neuro-Psychopharmacology and Biological Psychiatry 2013; 46: 153-60

View review abstract online

Comparison	**Semantic inhibition in people with bipolar disorder vs. controls compared to people with schizophrenia vs. controls**
Summary of evidence	**Moderate quality evidence (medium-sized samples, mostly consistent and precise, direct) suggests similar, medium to large effects of poor semantic inhibition in people with bipolar disorder and schizophrenia when compared to controls.**

Semantic inhibition

Significant, medium to large effects of poor semantic inhibition in both bipolar disorder and schizophrenia compared to controls on the following tasks;

Total Latency of Task A

Bipolar disorder: 6 studies, N = 341, *d* = 0.719, 95%CI 0.231 to 1.207, $p < 0.05$, Q$p < 0.01$

Schizophrenia: 7 studies, N = 405, *d* = 0.749, 95%CI 0.367 to 1.132, $p < 0.05$, Q$p < 0.01$

Total Latency of Task B

Bipolar disorder: 5 studies, N = 253, *d* = 0.930, 95%CI 0.403 to 1.457, $p < 0.05$, Q$p < 0.05$

Schizophrenia: 4 studies, N = 245, *d* = 0.840, 95%CI 0.566 to 1.113, $p < 0.05$, Q$p > 0.05$

Total Error of Task B

Bipolar disorder: 5 studies, N = 253, *d* = 0.866, 95%CI 0.402 to 1.330, $p < 0.05$, Q$p < 0.05$

Schizophrenia: 8 studies, N = 447, *d* = 0.944, 95%CI 0.698 to 1.190, $p < 0.05$, Q$p > 0.05$

Type A Error of Task B

Bipolar disorder: 2 studies, N = 146, *d* = 0.678, 95%CI 0.336 to 1.021, $p < 0.05$, Q$p < 0.05$

Schizophrenia: 6 studies, N = 395, *d* = 0.639, 95%CI 0.431 to 0.847, $p < 0.05$, Q$p > 0.05$

Significant, small effect of poor task performance in schizophrenia vs. controls only;

Type B Error of Task B

Bipolar disorder: 2 studies, N = 146, *d* = 0.869, 95%CI -0.472 to 2.211, $p > 0.05$, Q$p < 0.05$

Schizophrenia: 6 studies, N = 395, *d* = 0.170, 95%CI 0.578 to 0.247, 0.912, $p < 0.05$, Q$p < 0.05$

No significant differences between bipolar disorder or schizophrenia vs. controls;

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Suppression Time Bipolar disorder: 4 studies, N = 218, *d* = 0.156, 95%CI 0.240 to -0.313, *p* > 0.05, Q*p* < 0.05 Schizophrenia: 5 studies, N = 285, *d* = 0.325, 95%CI -0.065 to 0.549, *p* > 0.05, Q*p* < 0.05	
Consistency in results	Inconsistent, apart from Total Latency of Task B, Total Error of Task B, and Type A Error of Task B in schizophrenia.
Precision in results	Precise, apart from Type B Error of Task B in bipolar disorder.
Directness of results	Direct

Explanation of acronyms

CI = confidence interval, *d* = Cohen's standardised mean difference, EOS = early onset schizophrenia, *g* = Hedges' standardised mean difference, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), N = number of participants, *p* = probability of rejecting a null hypothesis of no differences between groups, PBD = paediatric bipolar disorder, Q = test for heterogeneity, SMD = standardised mean difference, vs. = versus

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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[10].

† 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[10].

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[11]. 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

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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[10];

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

§ 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[12].

‖ 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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