TECHNICAL COMMENTARY

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Schizophrenia and bipolar disorder

Introduction

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.

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. People with bipolar disorder may show similar symptoms to schizophrenia, such as psychotic features and depression which may result in misdiagnosis. Affective psychoses include psychotic depression, psychotic bipolar disorder and mania.

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 2000 that report results separately for people with a diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder or first episode schizophrenia. Reviews were identified by searching the databases MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO and the Cochrane library. Hand searching reference lists of identified reviews was also conducted. When multiple copies of reviews were found, only the most recent version 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 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.

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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 (RCT) 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 NeuRA (Neuroscience Research Australia).

Results

We found ten systematic reviews that met our inclusion criteria[3-12].

Executive functioning and language:

- High quality evidence shows a medium effect of lower performance on verbal fluency and executive control tasks in schizophrenia compared to bipolar disorder. Moderate quality evidence suggests this finding may also be applicable to concept formation.
- Moderate to high quality evidence shows a small effect of lower performance in schizophrenia on Trail Making Test (TMT)-A, TMT-B, and Wisconsin Card Sorting Task (WCST) categories tasks, but not on WCST perseverative errors or STROOP Colour and Word Test (SCWT) compared to bipolar disorder.
- Compared to people with affective psychosis, high quality evidence shows a small effect of lower performance on the WCST in people with schizophrenia, particularly those with increased negative symptoms, or fewer years of education. These findings apply when comparing schizophrenia to schizoaffective disorder, although to a lesser extent.
- High quality evidence shows medium-sized effect of poorer verbal fluency in people with first-episode schizophrenia compared to people with first-episode bipolar disorder.

Memory and learning:

- High quality evidence shows a medium effect of lower performance on verbal immediate, verbal delayed, and visual delayed memory in people with schizophrenia compared to people with bipolar disorder. Moderate quality evidence suggests this finding may also be applicable to verbal working memory, but not visual immediate memory.
- Moderate to high quality evidence shows a small effect of lower performance on the California Verbal Learning Test total free recall subscale, but not on the long delayed free recall or recognition hits subscales in patients with schizophrenia compared to bipolar disorder.
- High quality evidence shows medium-sized effects of poorer verbal memory in people with first-episode schizophrenia compared to people with first-episode bipolar disorder. Moderate quality evidence also shows a small effect of poorer working memory.

Psychomotor performance:

- Moderate quality evidence suggests a small to medium effect of lower performance on mental or psychomotor speed tasks in people with schizophrenia compared to people with affective psychosis or

schizoaffective disorder. No difference in fine motor skills is reported from high quality evidence.

- Moderate quality evidence shows a small effect of poorer psychomotor speed in people with first-episode schizophrenia compared to people with first-episode bipolar disorder.

IQ and global cognition:

- 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 compared to first-episode bipolar disorder.
- Moderate to high quality evidence finds a medium-sized effect of poorer pre-onset cognitive functioning and a large effect of poorer post-onset cognitive functioning in people with schizophrenia compared to controls. In people with bipolar disorder, there was a small effect of poorer pre-onset cognitive functioning and a medium-sized effect of poorer post-onset cognitive functioning compared to controls.
- Moderate quality evidence suggests a small to medium effect of lower IQ (but not premorbid IQ) in schizophrenia compared to affective psychosis or schizoaffective disorder.
- Moderate quality evidence shows a small effect of poorer global cognition in people with first-episode schizophrenia compared to people with first-episode bipolar disorder.

Social cognition:

- 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 for male patients. There were no differences on positive (happy) facial emotion recognition tasks.

Semantic inhibition

- Moderate quality evidence finds similar, medium to large effects of poor semantic inhibition in people with bipolar disorder and schizophrenia when compared to controls.

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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 schizophrenia vs. people with first-episode bipolar disorder.**
Summary of evidence	***Memory:*** **High quality evidence (large samples, consistent, precise, direct) shows medium-sized effects 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.** ***Verbal fluency:*** **High quality evidence shows medium-sized effect of poorer verbal fluency in people with first-episode schizophrenia compared to people with first-episode bipolar disorder.** ***Psychomotor performance:*** **Moderate quality evidence (inconsistent) shows a small effect of poorer psychomotor speed in people with first-episode schizophrenia compared to people with first-episode bipolar disorder.** ***IQ:*** **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 (imprecise and inconsistent) also shows a medium-sized effect of poorer current IQ in people with first-episode schizophrenia.** ***Global cognition:*** **Moderate quality evidence (inconsistent) 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	
A significant, small to medium-sized effect of poorer verbal 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 Learning: 5 studies, N = 638, *d* = 0.59, 95%CI 0.40 to 0.78, *p* < 0.001, I^2 not reported Recall: 5 studies, N = 638, *d* = 0.38, 95%CI 0.20 to 0.55, *p* < 0.001, I^2 not reported 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.	
Psychomotor speed	
A significant, small to medium-sized effect of poorer psychomotor speed in people with first-episode schizophrenia compared with first-episode bipolar disorder; All psychomotor 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.	
IQ	
A significant, medium-sized effect 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	
A significant, medium-sized effect 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, all verbal memory tasks, all working memory tasks, visual memory, all psychomotor tasks, TMT A, premorbid IQ, all fluency tasks, and letter fluency. Imprecise for TMT B, digit symbol, current IQ, category fluency, attention, 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
Directness of results	Direct

Bora E, Yucel M, Pantelis C

Cognitive functioning in schizophrenia, schizoaffective disorder and affective psychoses: meta-analytic study

The British Journal of Psychiatry 2009; 195: 475-482

View review abstract online

Comparison	**Cognitive functioning in people with schizophrenia vs. people with affective psychosis or schizoaffective disorder.** **Note: the schizophrenia group had more males, with a younger mean age and with fewer years of education, which may account for any observed effects.**
Summary of evidence	***Executive functioning:*** **Moderate to high quality evidence (unclear sample sizes, direct, precise, consistent) shows a small effect of worse performance on the Wisconsin Card Sorting Task in people with schizophrenia compared to people with affective psychosis, and to a lesser extent, compared to people with schizoaffective disorder.** **Moderate quality evidence (inconsistent) suggests this may also be applicable to the Trial Making Test Part B, but only in the comparison with affective psychosis.** ***Memory:*** **Moderate to high quality evidence (unclear sample sizes, direct, precise, some inconsistencies) shows a small effect of lower performance on verbal memory tasks in people with schizophrenia compared to people with affective psychosis and schizoaffective disorder. No differences in visual memory, spatial working memory or digit span tasks.**

	Psychomotor performance: **Moderate quality evidence (unclear sample sizes, inconsistent precise, direct) suggests a small effect of lower performance on psychomotor speed tasks in people with schizophrenia compared to people with affective psychosis or schizoaffective disorder.** ***IQ:*** **Moderate quality evidence (unclear sample sizes, inconsistent precise, direct) also suggests a small significant effect of lower performance on the Wechsler Adult Intelligence Scale IQ test in schizophrenia compared to affective psychosis or schizoaffective disorder.** **Note: Authors state that the observed group differences were driven by a higher percentage of males, more severe negative symptoms and younger age at onset of disorder in the schizophrenia samples.**
Executive functioning	
A significant, small effect suggests worse executive functioning in people with schizophrenia compared to people with affective psychosis or schizoaffective disorder; 19 studies (N not reported), d = 0.23, 95%CI 0.08 to 0.38, p = 0.003, Q_W p = 0.002 *Subgroup analysis shows that this effect is only significant when compared to affective psychosis, and not when compared to schizoaffective psychosis;* Schizophrenia vs. affective psychosis: 12 studies, d = 0.28, 95%CI 0.11 to 0.46, p = 0.002, Q_W p = 0.04 Schizophrenia vs. schizoaffective disorder: 9 studies, d = 0.12, 95%CI -0.06 to 0.31, p = 0.19, Q_W p = 0.11 *Subgroup analysis shows that the effect sizes were non-significant when using only gender-matched studies, and that heterogeneity was substantially reduced (statistics not reported).* Results for individual executive functioning tasks: *Wisconsin Card Sorting Test – worse performance in schizophrenia for all comparisons;* Schizophrenia vs. affective psychosis/schizoaffective: 15 studies, d = 0.25, 95%CI 0.12 to 0.38, p < 0.05, Q_W p = 0.39 Schizophrenia vs. affective psychosis: 9 studies, d = 0.30, 95%CI 0.10 to 0.50, p = 0.004, Q_W p = 0.20 Schizophrenia vs. schizoaffective disorder: 7 studies, d = 0.21, 95%CI 0.03 to 0.39, p = 0.02, Q_W p = 0.57	

Trial Making Test Part B – worse performance in schizophrenia vs. affective psychosis only; Schizophrenia vs. affective psychosis/schizoaffective: 10 studies, *d* = 0.23, 95%CI 0.00 to 0.47, *p* = 0.06, Q_W *p* = 0.001 Schizophrenia vs. affective psychosis: 8 studies, *d* = 0.27, 95%CI 0.01 to 0.52, *p* = 0.04, Q_W *p* = 0.009 Schizophrenia vs. schizoaffective disorder: 5 studies, *d* = 0.17, 95%CI -0.15 to 0.49, *p* = 0.30, Q_W *p* = 0.24 *Meta-regression to investigate significant heterogeneity in the overall analysis showed that schizophrenia samples with more severe negative symptoms (particularly males), or fewer years of education showed the greatest impairments compared to affective psychosis/schizoaffective;* Negative symptoms: 6 studies, B = 0.41, SE = 0.09, *p* < 0.001 Years of education (number of studies not reported): B = 0.89, SE = 0.30, *p* = 0.003	
Consistency in results	Consistent for schizophrenia vs. schizoaffective disorder subgroup analyses and Wisconsin Card Sorting Test only
Precision in results	Precise
Directness of results	Direct
Memory	
A significant, small effect suggests worse overall memory performance in people with schizophrenia compared to people with affective psychosis or schizoaffective disorder; 13 studies (N = not reported), *d* = 0.27, 95%CI 0.11 to 0.43, *p* = 0.001, Q_W, *p* = 0.12 *Subgroup analysis shows that this effect is significant for both comparisons with affective psychosis and with schizoaffective psychosis;* Schizophrenia vs. affective psychosis: 7 studies, *d* = 0.30, 95%CI 0.05 to 0.55, *p* = 0.02, Q_W *p* = 0.07 Schizophrenia vs. schizoaffective disorder: 6 studies, *d* = 0.23, 95%CI 0.04 to 0.43, *p* = 0.02, Q_W *p* = 0.35 *Subgroup analysis shows that the effect sizes were non-significant when using only gender-matched studies, and that heterogeneity was substantially reduced (statistics not reported);* Results for individual memory tasks: *Verbal memory – worse performance in schizophrenia for all comparisons;* Schizophrenia vs. affective psychosis: 6 studies, *d* = 0.36, 95%CI 0.03 to 0.69, *p* = 0.003, Q_W *p* = 0.001 Schizophrenia vs. schizoaffective disorder: 4 studies, *d* = 0.23, 95%CI 0.02 to 0.44, *p* = 0.03, Q_W *p* = 0.55	

Immediate verbal memory: 8 studies, *d* = 0.42, 95%CI 0.20 to 0.65, *p* < 0.05, Q_W *p* = 0.02 Verbal working memory: 7 studies, *d* = 0.31, 95%CI 0.02 to 0.57, *p* < 0.05, Q_W *p* = 0.06 Verbal memory delay: 9 studies, *d* = 0.29, 95%CI 0.09 to 0.49, *p* < 0.05, Q_W *p* = 0.07 *Visual memory – no differences for any comparison;* Schizophrenia vs. affective psychosis: 5 studies, *d* = 0.10, 95%CI -0.27 to 0.46, *p* = 0.60, Q_W *p* = 0.01 Schizophrenia vs. schizoaffective disorder: 4 studies, *d* = 0.08, 95%CI -0.35 to 0.51, *p* = 0.72, Q_W *p* = 0.02 Immediate visual memory: 4 studies, *d* = 0.14, 95%CI -0.21 to 0.50, *p* = 0.43, Q_W *p* = 0.03 Visual memory delay: 8 studies, *d* = 0.09, 95%CI -0.24 to 0.40, *p* = 0.63, Q_W *p* < 0.001 *No differences for spatial working memory or digit span;* Spatial working memory: 4 studies, *d* = -0.09, 95%CI -0.55 to 0.38, *p* = 0.71, Q_W *p* = 0.09 Digit span: 12 studies, *d* = 0.02, 95%CI -0.14 to 0.18, *p* = 0.78, Q_W *p* = 0.17 *Meta-regression of the overall analysis showed that schizophrenia samples with more severe negative symptoms showed the greatest impairments compared to people with schizoaffective/ affective psychosis;* 5 studies, B = 0.23, SE = 10, *p* = 0.02	
Consistency	Consistent for overall memory, schizoaffective subgroup analysis for verbal memory, spatial working memory and digit span only
Precision	Precise
Directness	Direct
Psychomotor speed	
A significant, small effect suggests worse psychomotor speed in people with schizophrenia compared to people with affective psychosis or schizoaffective disorder; 17 studies (N = not reported), *d* = 0.24, 95%CI 0.07 to 0.42, *p* = 0.0055, Q_W, *p* = 0.001 *Subgroup analysis shows that this effect is significant for both comparisons with affective psychosis and with schizoaffective psychosis;* Schizophrenia vs. affective psychosis: 11 studies, *d* = 0.27, 95%CI 0.03 to 0.51, *p* = 0.03, Q_W *p* = 0.001 Schizophrenia vs. schizoaffective disorder: 8 studies, *d* = 0.22, 95%CI 0.02 to 0.43, *p* = 0.03, Q_W *p* = 0.05 *Subgroup analysis shows that the effect sizes were non-significant when using only gender-matched studies (statistics not reported).*	

Results for individual psychomotor speed tasks: *Verbal fluency (authors report that this task is highly correlated with mental speed tasks, so is indicative of mental speed) – trend for worse performance in schizophrenia for all comparisons;* Schizophrenia vs. affective psychosis/schizoaffective: 9 studies, *d* = 0.22, 95%CI -0.03 to 0.48, *p* = 0.09, Q_W *p* = 0.002 Schizophrenia vs. affective psychosis: 6 studies, *d* = 0.29, 95%CI -0.01 to 0.59, *p* = 0.06, Q_W *p* = 0.01 Schizophrenia vs. schizoaffective disorder: 5 studies, *d* = 0.32, 95%CI 0.00 to 0.64, *p* = 0.05, Q_W *p* = 0.15 *Mental speed - worse performance in schizophrenia for all comparisons;* Schizophrenia vs. affective psychosis/schizoaffective: 12 studies, *d* = 0.26, 95%CI 0.03 to 0.49, *p* < 0.05, Q_W *p* < 0.0001 Schizophrenia vs. affective psychosis: 8 studies, *d* = 0.26, 95%CI -0.10 to 0.61, *p* = 0.15, Q_W *p* < 0.0001 Schizophrenia vs. schizoaffective disorder: 5 studies, *d* = 0.24, 95%CI 0.01 to 0. 47, *p* = 0.04, Q_W *p* = 0.02 *Meta-regression showed that schizophrenia samples with more severe symptoms, fewer years of education and younger age showed the greatest impairments compared to people with schizoaffective/ affective psychosis;* Negative symptoms: 6 studies, B = 0.39, SE = 0.09, *p* < 0.001 Positive symptoms: 20 studies, B = 0.59, SE = 0.29, *p* = 0.04 Fewer years of education (number of studies not reported): B = 0.69, SE = 0.32, *p* = 0.03 Younger age: 10 studies, B = 0.17, SE = 0.19, *p* = 0.05
IQ
A small significant effect of worse performance on the Wechsler Adult Intelligence Scale IQ test in schizophrenia compared to affective psychosis or schizoaffective disorder; 7 studies, *d* = 0.37, 95%CI 0.09 to 0.65, *p* < 0.009, Q_W *p* < 0.03

Consistency	Inconsistent
Precision	Precise
Directness	Direct

Daban C, Martinez-Aran A, Torrent C, Tabarés-Seisdedos R, Balanzá-Martínez V, Salazar-Fraile J, Selva-Vera G, Vieta E

Specificity of cognitive deficits in bipolar disorder versus schizophrenia: A systematic review

Psychotherapy and Psychosomatics 2006;75: 72-84

View review abstract online

Comparison	**Cognitive performance in people with schizophrenia vs. people with bipolar disorder.**
Summary of evidence	**Moderate quality evidence (medium to large samples, unable to assess consistency or precision, direct) suggests people with schizophrenia may show impaired IQ (not premorbid), immediate story recall and psychosocial functioning compared to people with bipolar disorder.**

Psychosocial functioning and IQ

2 studies (N = 198) reported more impaired *psychosocial functioning* in people with schizophrenia compared to people with bipolar disorder.

7 studies (N = 767) reported lower *IQ* scores (WAIS) in people with schizophrenia compared to people with bipolar disorder. 1 study (N = 137) reported no differences between groups.

6 studies reported lower *premorbid IQ* (NART 4 studies, N = 706; WAIS-R vocabulary 2 studies, N = 269) in people with schizophrenia compared to people with bipolar disorder. However, 8 studies (N = 818) reported no differences (NART, WRAT-R, WAIS-R vocabulary). Both groups performed worse than controls. 3 longitudinal studies reported no differences at baseline in adolescence later diagnosed with schizophrenia or bipolar disorder.

Attention

2 studies (N = 327) reported worse *sustained attention* (CPT performance) in people with schizophrenia compared to people with bipolar disorder. However, 4 studies (N = 405) reported no difference in CPT performance. Both groups performed worse than controls.

3 studies (N = 325) reported worse *selective attention* (SCWT performance) in people with schizophrenia compared to bipolar disorder. However, 6 studies (N = 816) reported no difference in SCWT performance. Both groups performed worse than controls. 2 studies (N = 279) reported no difference between people with schizophrenia or bipolar disorder without psychotic symptoms. 1 study (N = 108) reported worse performance in people with affective disorder with psychotic symptoms compared to people with affective disorder without psychotic symptoms. 2 studies reported an association between increased symptom severity (particularly negative symptoms) and worse selective attention.

Memory	
6 studies (N = 831) reported worse *immediate story recall* in people with schizophrenia compared to people with bipolar disorder. 1 study (N = 446) reported that both groups were impaired compared to controls. Only 1 study, (N = 102) reported worse *verbal memory* (WMS-R logical memory and paired associates) in people with schizophrenia compared to people to people with unipolar or depressive bipolar. 8 studies (N = 721) reported no difference in verbal memory (CVLT, AVLT, WMS-R logical memory and paired associates, Babcock story recall) in people with schizophrenia compared to bipolar disorder. 3 studies, (N = 246) reported both groups showed impaired performance compared to controls. 1 study, (N = 223) reported worse verbal memory in people with first-admission schizophrenia than in people with first-admission psychotic affective disorder. 5 studies (N = 466) reported no difference in *working memory* (Visual Backward Masking task) in people with schizophrenia and bipolar disorder.	
Executive functioning	
8 studies (N = 872) reported worse executive functioning (WCST) in people with schizophrenia compared to people with bipolar disorder. However, 9 studies (N = 953) reported no differences in WCST performance. 1 study (N = 107) reported an association between increase negative symptoms and poorer performance. 3 studies (N = 226) reported that people with schizophrenia showed worse WCST categories performance but similar perseverative errors than people with bipolar disorder. 6 studies (N = 729) reported impaired TMT-B performance in people with schizophrenia compared to people with bipolar disorder. However, 8 studies (N = 707) reported no difference in TMT-B performance. 1 study (N = 108) reported that people with psychotic symptoms performed more poorly than those without psychotic symptoms.	
Language	
6 studies (N = 651) reported worse *verbal fluency* in people with schizophrenia compared to people with bipolar disorder. However, 5 studies (N = 405) reported no difference in *verbal fluency* between people with schizophrenia and people with bipolar disorder. 4 studies, (N = 291) report that both groups were impaired compared to controls. 1 study (N = 94) reported an association between increased negative symptoms and worse verbal fluency.	
Consistency	Unable to formally assess consistency – appears mostly inconsistent
Precision	Unable to assess precision – CIs not provided
Directness	Direct

Krabbendam L, Arts B, van Os J, Aleman A

Cognitive functioning in patients with schizophrenia and bipolar disorder: A quantitative review

Schizophrenia Research 2005; 80: 137-149

View review abstract online

Comparison	**Cognitive performance in people with schizophrenia vs. people with bipolar disorder.**
Summary of evidence	***Executive functioning:*** **High quality evidence (large samples, consistent, precise, direct) shows a medium-sized effect of lower performance on verbal fluency and executive control tasks in studies that have matched samples on remission status, duration of disorder / number of admissions, and age / education variables. Moderate to high quality evidence (inconsistent) suggests this finding may also be applicable to concept formation with evidence from matched or unmatched studies.** ***Memory:*** **High quality evidence (large samples, consistent, precise, direct) shows a medium effect of lower performance on verbal immediate, verbal delayed and visual delayed memory in people with schizophrenia compared to people with bipolar disorder. Moderate to high quality evidence (inconsistent) suggests this finding may also be applicable to verbal working memory but not visual immediate memory.** ***Psychomotor:*** **Moderate to high quality evidence (large samples, inconsistent, precise, direct) suggests a medium effect of lower performance in mental speed in people with schizophrenia compared to people with bipolar disorder. No difference in fine motor skills is reported from high quality evidence.** ***IQ:*** **Moderate to high quality evidence (large samples, inconsistent, precise, direct) suggests a small to medium effect of lower performance in IQ in people with schizophrenia compared to people with bipolar disorder.**

Executive functioning (executive control, concept formation and fluency)
A significant, medium effect suggests people with schizophrenia showed impaired performance on executive functioning tasks compared to people with bipolar disorder;
Verbal fluency: 11 studies, N = 823, *d* = 0.63, 95%CI 0.40 to 0.85, *p* < 0.0001, Q_w = 22.3, *p* = 0.01
Executive control: 11 studies, N = 801, *d* = 0.55, 95%CI 0.19 to 0.91, *p* = 0.002, Q_w = 52.5, *p* < 0.001
Concept formation: 17 studies, N = 1,158, *d* = 0.34, 95%CI 0.11 to 0.57, *p* = 0.004, Q_w = 51.0, *p* < 0.0001
Results were similar and across study heterogeneity was reduced in subgroup analyses of studies matched for remission status, duration of disorder / number of admissions, and age / education on fluency and executive control.
In remission: 10 studies, N = 646, *d* = 0.49, 95%CI 0.28 to 0.70, *p* = 0.0001, Q_w = 14.3, *p* = 0.11
Duration of disorder / number of admissions: 10 studies, N = 832, *d* = 0.49, 95%CI 0.31 to 0.67, *p* < 0.0001, Q_w = 12.6, *p* = 0.19
Age / education: 10 studies, N = 702, *d* = 0.50, 95%CI 0.29 to 0.71, *p* = 0.0001, Q_w = 14.8, *p* = 0.10
Memory
A significant, medium effect suggests people with schizophrenia showed more impaired performance on the following memory components compared to people with bipolar disorder;
Verbal working memory: 8 studies, N = 532, *d* = 0.60, 95%CI 0.12 to 1.07, *p* = 0.01, Q_w = 38.0, *p* < 0.001
Verbal immediate memory: 9 studies, N = 697, *d* = 0.43, 95%CI 0.23 to 0.63, *p* < 0.0001, Q_w = 11.6, *p* = 0.17
Verbal delayed memory: 7 studies, N = 523, *d* = 0.34, 95%CI 0.16 to 0.53, *p* = 0.0003, Q_w = 3.6, *p* = 0.73
Visual delayed memory: 4 studies, N = 360, *d* = 0.51, 95%CI 0.25 to 0.76, *p* = 0.0009, Q_w = 3.8, *p* = 0.28
But not on visual immediate memory: 5 studies, N = 431, *d* = 0.26, 95%CI -0.12 to 0.64, *p* = 0.17, Q_w = 11.9, *p* = 0.02
Psychomotor skills
A significant, medium effect suggests people with schizophrenia showed more impaired performance on mental speed compared to people with bipolar disorder;
Mental speed: 11 studies, N = 872, *d* = 0.50, 95%CI 0.10 to 0.89, *p* = 0.01, Q_w = 70.5, *p* < 0.001
But not on fine motor skills: 4 studies, N = 339, *d* = 0.06, 95%CI -0.16 to 0.27, *p* = 0.61, Q_w = 3.0, *p* = 0.39

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IQ	
A significant small to medium effect suggests people with schizophrenia showed impaired performance on various cognitive tests compared to people with bipolar disorder; IQ: 7 studies, N = 338, *d* = 0.36, 95%CI 0.01 to 0.71, *p* = 0.04, Q_w = 13.6, *p* = 0.03	
Consistency	Inconsistent for all except visual delayed memory, verbal immediate memory, verbal delayed memory, fine motor skills and subgroup analyses
Precision	Precise
Directness	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. controls.**
Summary of evidence	**EOS vs. controls:** **High quality evidence (consistent, precise, direct, large samples) suggests a large effect of poor attention, working memory, verbal fluency, verbal learning and memory and visual memory in EOS.** **Moderate to high quality evidence (imprecise or inconsistent) suggests a large effect of poor general cognitive ability, visuospatial ability, processing speed, executive control, and a medium effect of poor motor skills in EOS.** **PBD vs. controls:** **High quality evidence suggests a large effect of poor processing speed, and a medium effect 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) suggests a medium 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 males in both diagnostic groups.

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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

Quraishi S, Frangou S

Neuropsychology of bipolar disorder: a review

Journal of Affective Disorders 2002; 72: 209-225

View review abstract online

Comparison	**Cognitive performance in people with schizophrenia vs. bipolar disorder.**
Summary of evidence	**Moderate to low quality evidence (mostly inconsistent, unable to assess precision, medium to large samples, direct) suggests IQ may be more impaired in schizophrenia than in bipolar disorder.**

	The results for the other cognitive constructs are very inconsistent.
Executive functioning	
5 studies reported lower executive functioning performance in people with schizophrenia compared to people with bipolar disorder (some samples also include unipolar depression), however 3 studies (N = 344) reported no differences between groups. 1 study (N = 81) reported impaired executive functioning in people with psychotic bipolar but not people with schizophrenia.	
Memory	
1 study (N = 223) reported impaired WMS-R performance in people with schizophrenia compared to people with bipolar disorder and unipolar depression. 1 study (N = 65) reported no difference between people with schizophrenia and bipolar disorder on the BVRT or WMS.	
Attention	
4 studies reported worse attention in people with schizophrenia than in people with bipolar disorder, including lower attention performance on SPAN (N = 75), WMS (N = 102), SCWT (N = 66), and TMT and SCWT (N = 223). However, 5 studies reported no significant difference in attention between groups, including overall attention performance (N = 81), performance on digit span (N = 77), TMT (N = 65), letter detection (N = 35), and SCWT (N = 101).	
IQ	
6 studies reported lower IQ in people with schizophrenia compared to people with bipolar disorder, including general intelligence (2 studies, N = 216), reading (1 study, N = 308), full-scale IQ (1 study, N = 111) and verbal IQ (2 studies, N = 223). 1 study (N = 65) on general intelligence and another on performance IQ (N = 112) reported no differences between groups.	
Consistency	Unable to assess – no measure of consistency is reported.
Precision	Unable to assess – CIs not provided
Directness	Direct

Stefanopoulou E, Manoharan A, Landau S, Geddes J, Goodwin G, Frangou S

Cognitive functioning in patients with affective disorders and schizophrenia: A meta-analysis

International Review of Psychiatry 2009; 21(4):336-356 View review abstract online	
Comparison	**Cognitive performance in people with schizophrenia vs. bipolar disorder.**
Summary of evidence	***Executive functioning & attention:*** **Moderate to high quality evidence (unclear sample sizes, direct, consistent, precise) shows a small effect of lower performance on TMT-A, TMT-B, and WCST categories, but not on WCST perseverative errors or the STROOP test in patients with schizophrenia compared to patients with bipolar disorder.** ***Verbal memory & learning:*** **Moderate to high quality evidence (unclear sample sizes, direct, consistent, precise) shows a small effect of lower performance on the California Verbal Learning Test total free recall subscale, but not on the long delayed free recall or recognition hits subscales in patients with schizophrenia vs. bipolar disorder. A small effect was also reported for poorer language performance on the Controlled Oral Word Association Test.** ***IQ:*** **Moderate quality evidence (unclear sample sizes, direct, some inconsistencies, precise) suggests a medium effect of lower IQ in schizophrenia compared to bipolar disorder.**
Executive functioning & attention	
A significant, small effect suggests people with schizophrenia were more impaired on the following tests than people with bipolar disorder; TMT-A: (number of studies not reported) SMD = -0.23, 95%CI -0.44 to 0.03, p = 0.02, I^2 = not reported, p = 0.06 TMT-B: SMD = -0.42, 95%CI -0.63 to 0.21, $p < 0.0001$, I^2 = not reported, p = 0.08 WCST Categories achieved: SMD = 0.37, 95%CI 0.22 to 0.51, $p < 0.0001$, I^2 = not reported, p = 0.30 However, no differences were reported for the following tests: WCST perseverative errors: SMD = -0.14, 95%CI -0.33 to 0.03, p = 0.10, I^2 = not reported, p = 0.14 Stroop Colour Word Test: SMD = 0.18, 95%CI -0.16 to 0.58, p = 0.34, I^2 = not reported, p = 0.21	
Verbal memory & learning	

A significant, small effect suggests that people with schizophrenia had lower performance on the California Verbal Learning Test total free recall subscale compared to people with bipolar disorder However, no differences were reported on the long delayed free recall and recognition hits subscales; Total free recall: (number of studies not reported) SMD = 0.39, 95%CI 0.06 to 0.72, p = 0.02, I^2 = not reported, p = 0.71 Long delayed free recall: SMD = 0.16, 95%CI -0.16 to 0.48, p = 0.33, I^2 = not reported, p = 0.73 Recognition hits: SMD = 0.07, 95%CI -0.31 to 0.47, p = 0.69, I^2 = not reported, p = 0.50 *A significant, small effect suggests that people with schizophrenia produced fewer words on the Controlled Oral Word Association Test compared to people with bipolar disorder;* SMD = 0.35, 95%CI 0.14 to 0.55, p = 0.001, I^2 = not reported, p = 0.06
IQ
A significant, medium effect suggests that people with schizophrenia had lower IQ scores than people with bipolar disorder WAIS general intelligence: (number of studies not reported) SMD = 0.69, 95%CI 0.50 to 0.87, p < 0.0001, I^2 = not reported, p = 0.27 WAIS verbal IQ: SMD = 0.56, 95%CI 0.14 to 0.99, p = 0.009, I^2 = 71%, p = 0.004 WAIS performance IQ: SMD = 0.52, 95%CI 0.14 to 0.90, p = 0.007, I^2 = 63.4%, p = 0.01 *No difference in reading scores was reported between people with schizophrenia and people with bipolar disorder;* NART: SMD = 0.27, 95%CI -0.18 to 0.73, p = 0.24, I^2 = 60.5%, p = 0.05

Consistency	Unable to assess – no measure of consistency is reported.
Precision	Unable to assess – CIs not provided
Directness	Direct

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

AVLT = Auditory Verbal Learning Test, B = estimated regression coefficient , BVRT = Benton Visual Retention Test, CI = Confidence Interval, CPT = Continuous Performance Test, CVLT = California Verbal Learning Test, *d* = Cohen's *d* and *g* = Hedges' *g* = standardised mean differences (see below for interpretation of effect size), EOS = early onset schizophrenia, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), IQ = intelligence quotient, N = number of participants, NART = National Adult Reading Test, *p* = statistical probability of obtaining that result (*p* < 0.05 generally regarded as significant), PBD = paediatric bipolar disorder, Q = Q statistic for the test of heterogeneity, Q_w = test for within group differences (heterogeneity in study results within a group of studies – measure of study consistency), Q_B = test for between group differences (heterogeneity between groups of studies for an outcome of interest), RAVLT = Rey Auditory Verbal Learning Test, SCWT = Stroop Colour and Word Test, SE = standard error, SMD = standardised mean difference, TMT = Trail Making Test, vs = versus, WAIS = Wechsler Adult Intelligence Scale, WAIS-R = Wechsler Adult Intelligence Scale-Revised, WCST = Wisconsin Card Sorting Task, WMS-R = Wechsler Memory Scale- Revised, WRAT-R = Wide Range Achievement Test- Revised

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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.[13]

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† 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.[13]

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[14]. 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[13];

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

§ 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.[15]

‖ 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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References

1. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMAGroup (2009): Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *British Medical Journal* 151: 264-9.
2. GRADEWorkingGroup (2004): Grading quality of evidence and strength of recommendations. *British Medical Journal* 328: 1490.
3. Bora E, Yucel M, Pantelis C (2009): Cognitive functioning in schizophrenia, schizoaffective disorder and affective psychoses: meta-analytic study. *British Journal of Psychiatry* 195: 475-82.
4. Daban C, Martinez-Aran A, Torrent C, Tabares-Seisdedos R, Balanza-Martinez V, Salazar-Fraile J*, et al.* (2006): Specificity of cognitive deficits in bipolar disorder versus schizophrenia. A systematic review. *Psychotherapy and Psychosomatics* 75: 72-84.
5. Krabbendam L, Arts B, van Os J, Aleman A (2005): Cognitive functioning in patients with schizophrenia and bipolar disorder: a quantitative review. *Schizophrenia Research* 80: 137-49.
6. Quraishi S, Frangou S (2002): Neuropsychology of bipolar disorder: a review. *Journal of Affective Disorders* 72: 209-26.
7. Stefanopoulou E, Manoharan A, Landau S, Geddes JR, Goodwin G, Frangou S (2009): Cognitive functioning in patients with affective disorders and schizophrenia: a meta-analysis. *International Review of Psychiatry* 21: 336-56.
8. Nieto RG, Xavier Castellanos F (2012): A meta-analysis of neuropsychological functioning in patients with early onset schizophrenia and pediatric bipolar disorder. *Journal of Clinical Child and Adolescent Psychology* 40: 266-80.
9. Bora E, Pantelis C (2015): Meta-analysis of cognitive impairment in first-episode bipolar disorder: Comparison with first-episode schizophrenia and healthy controls. *Schizophrenia Bulletin* 41: 1095-104.
10. Bora E, Pantelis C (2016): Social cognition in schizophrenia in comparison to bipolar disorder: A meta-analysis. *Schizophrenia Research* 175: 72-8.
11. Wang K, Song LL, Cheung EFC, Lui SSY, Shum DHK, Chan RCK (2013): 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* 46: 153-60.
12. Trotta A, Murray RM, MacCabe JH (2015): Do premorbid and post-onset cognitive functioning differ between schizophrenia and bipolar disorder? A systematic review and meta-analysis. *Psychological Medicine* 45: 381-94.
13. CochraneCollaboration (2008): Cochrane Handbook for Systematic Reviews of Interventions. Accessed 24/06/2011.
14. Rosenthal JA (1996): Qualitative Descriptors of Strength of Association and Effect Size. *Journal of Social Service Research* 21: 37-59.
15. GRADEpro (2008): [Computer program]. Jan Brozek, Andrew Oxman, Holger Schünemann. *Version 32 for Windows*