

Attention

Introduction

Selective attention is the ability to focus on relevant stimuli and ignore irrelevant stimuli. Sustained attention is the ability to maintain a consistent focus. Selective and sustained attention involve 'alerting' (achieving and maintaining an alert state); 'orienting' (directing attention); and 'executive control' (choosing suitable responses).

Several tasks have been developed to assess attention performance. The most common tasks include the Continuous Performance Test (CPT) that uses both visual and auditory stimuli and requires participants to respond to targets and ignore distractors. The Trail Making Test (TMT), requires participants to connect, in order, letters and/or numbers as quickly as possible. The Stroop Colour Word Test (SCWT), presents colour names printed in an ink congruent to the colour name (e.g. blue), or incongruent to the colour name (e.g. blue). Participants are asked to either read the word or name the ink colour.

Any impairment in attention disrupts other cognitive functions. Information processing, for example, requires selective attention to retrieve relevant information, and dismiss irrelevant information. Working memory requires sustained attention in order to maintain concentration on information temporarily being stored. Therefore, tasks that have been developed to measure attention also measure other cognitive constructs.

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-analysis¹. Reviews with less than 50% of items checked have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

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

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Results

We found 12 systematic reviews that met our inclusion criteria³⁻¹⁴.

- Moderate to high quality evidence suggests a medium-sized effect of poorer attention in people with bipolar disorder compared to controls, with no significant changes over time (3-5 years). This effect was similar in bipolar I and bipolar II disorder, in people with first-episode bipolar disorder, and in elderly patients who were matched with controls for age and education. The effect was not significant in children with bipolar disorder who were matched to controls for age (mean 13 years) and IQ (mean score 104).
- High quality evidence suggests a small association between poorer attention and poorer general functioning in people with bipolar disorder.
- People with first-episode bipolar disorder showed a medium-sized effect of better performance on some attention tasks (TMT-A and B) compared to people with first-episode schizophrenia (moderate quality evidence). However, high quality evidence showed no differences in attention between people with bipolar disorder and a history of psychotic symptoms and people with bipolar disorder and no history of psychotic symptoms.
- Moderate quality evidence found no differences in attention between people with bipolar disorder and people with major depression, in both euthymic and depression phases.
- In people of any age with a first-degree relative with bipolar disorder, moderate to high quality evidence found no differences in attention compared to controls, or compared to first-degree relatives of people with schizophrenia. However, in youth aged 10 to 25 years with a first-degree relative with bipolar disorder, there was a small to medium-sized effect of poorer attention compared to controls.

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

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

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

[View review abstract online](#)

Comparison	Attention in people with bipolar disorder vs. controls.
Summary of evidence	Moderate to high quality evidence (large sample, inconsistent, precise, direct) suggests a medium-sized effect of poorer attention in people with bipolar disorder.
Attention	
<i>A significant, medium-sized effect of poorer attention in people with bipolar disorder; 7 studies, N = 487, d = -0.58, 95%CI -0.86 to -0.29, p < 0.05, I² = 78.9%, p < 0.001</i>	
Consistency in results[†]	Inconsistent
Precision in results[§]	Precise
Directness of results	Direct

Bora E, Pantelis C

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

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

[View review abstract online](#)

Comparison 1	Attention in people with first-episode bipolar disorder vs. controls.
Summary of evidence	Moderate to high quality evidence (medium-sized sample, consistent, precise, direct) suggests a medium to large effect of poorer attention in people with first-episode bipolar disorder.
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<p><i>A significant, medium to large effect of poorer attention in people with first-episode bipolar disorder; 3 studies, N = 262, d = 0.80, 95%CI 0.54 to 1.06, p < 0.001, I² = 0%, p = 0.96</i></p> <p>Authors report no evidence of publication bias.</p>	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct
Comparison 2	Attention in people with first-episode bipolar disorder vs. people with first-episode schizophrenia.
Summary of evidence	Moderate quality evidence (medium to large samples, inconsistent) shows a medium-sized effect of poorer attention on TMT-A and TMT-B tasks, but not other tasks in people with first-episode schizophrenia compared to people with first-episode bipolar disorder.
Attention	
<p><i>Significant, medium-sized impairment on TMT-A and TMT-B tasks in people with first-episode schizophrenia, with no differences on other tasks of attention;</i></p> <p>TMT-A: 3 studies, N = 328, d = 0.45, 95%CI 0.23 to 0.68, p < 0.001</p> <p>TMT-B: 3 studies, N = 328, d = 0.47, 95%CI 0.14 to 0.80, p = 0.006</p> <p>Other tasks: 2 studies, N = 101, d = 0.05, 95%CI -0.38 to 0.47, p = 0.83, I² = 0%, p = 0.62</p> <p>Authors report no evidence of publication bias.</p> <p>No differences were found for males vs. females or younger vs. older patients.</p>	
Consistency in results	Inconsistent for TMT A and B, consistent for other tasks.
Precision in results	Precise for TMT A, imprecise for TMT B and other tasks.
Directness of results	Direct

Bora E

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

European Psychiatry: the Journal of the Association of European Psychiatrists 2017; 45: 121-8

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Comparison 1	Attention in first-degree relatives of people with bipolar disorder vs. controls.
Summary of evidence	Moderate to high quality evidence (large samples, inconsistent, precise, direct) suggests no differences in sustained attention.
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<p><i>There were no differences in sustained attention;</i> 8 studies, N = 1,266, $d = 0.14$, 95%CI -0.08 to 0.37, $p = 0.21$, $I^2 = 72%$, $p = 0.002$ There was no evidence of publication bias.</p>	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct
Comparison 2	Attention in first-degree relatives of people with bipolar disorder vs. first-degree relatives of people with schizophrenia.
Summary of evidence	High quality evidence (large sample, consistent, precise, direct) suggests no differences in sustained attention.
Attention	
<p><i>There were no differences in sustained attention;</i> 8 studies, N = 1,450, $d = 0.11$, 95%CI -0.04 to 0.26, $p = 0.14$, $I^2 = 27%$, $p = 0.21$</p>	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Bora E, Ozerdem A

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

European Psychiatry 2017; 44: 17-23

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Comparison	Attention in first-degree relatives aged 10 to 25 years of a person with bipolar disorder vs. controls.
Summary of evidence	Moderate to high quality evidence (large sample, inconsistent, precise, direct) suggests a small to medium effect of poorer performance on sustained attention in young relatives of people with bipolar disorder.
Attention	
<p><i>Significant, small to medium-sized effect of poorer performance in sustained attention in young relatives of bipolar patients;</i></p> <p>5 studies, N = 618, $d = 0.36$, 95%CI 0.05 to 0.66, $p = 0.02$, $I^2 = 72%$, $p = 0.007$</p>	
Consistency	Inconsistent
Precision	Precise
Directness	Direct

<p><i>Bora E</i></p> <p>Neurocognitive features in clinical subgroups of bipolar disorder: A meta-analysis</p> <p>Journal of Affective Disorders 2018; 229: 125-34</p> <p>View review abstract online</p>	
Comparison	Attention in people with bipolar disorder and a history of psychotic symptoms vs. people with bipolar disorder and no history of psychotic symptoms.
Summary of evidence	High quality evidence (large samples, consistent, precise, direct) suggests no differences in attention.
Attention	
<p><i>There were no significant differences in attention;</i></p> <p>8 studies, N = 613, $d = 0.14$, 95%CI -0.02 to 0.31, $p = 0.09$, $I^2 = 0%$, $p = 0.98$</p> <p>There were no significant differences in effect sizes between euthymic and non-euthymic or bipolar I and II disorder samples.</p>	

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Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Bora E, McIntyre RS, Ozerdem A

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

Psychological medicine 2019; 49: 738-49

[View review abstract online](#)

Comparison	Attention in overweight people with bipolar disorder vs. normal weight people with bipolar disorder.
Summary of evidence	Moderate to high quality evidence (medium-sized sample, consistent, precise, direct) shows no differences in attention.
Attention	
<i>No significant differences between groups; 4 studies, N = 263, d = 0.37, 95%CI -0.03 to 0.57, p = 0.07, I² = 57%, p = 0.07</i>	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

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

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

Bipolar Disorders 2012; 14: 217-26

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Comparison	Associations between attention and functioning in people with bipolar disorder.
Summary of evidence	High quality evidence (large sample, consistent, precise, direct) suggests a small association between poor attention/vigilance and poor general functioning.
General functioning and attention	
<i>Significant, small association between poor attention/vigilance and poor general functioning; 9 studies, N > 336, r = 0.22, 95%CI 0.13 to 0.30, p < 0.0045, Qp = 0.833</i>	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Dickinson T, Becerra R, Coombes J

Executive functioning deficits among adults with Bipolar Disorder (types I and II): A systematic review and meta-analysis

Journal of Affective Disorders 2017; 218: 407-27

[View review abstract online](#)

Comparison	Attention in people with bipolar I disorder and bipolar II disorder vs. controls.
Summary of evidence	Moderate quality evidence (large sample, inconsistent, some imprecision, direct) suggests small to medium-sized effects of poorer attention in people with bipolar disorder compared to controls, with no differences between bipolar I disorder and bipolar II disorder.
Attention	
<i>Small to medium-sized trend effects show poorer performance on attention tasks in people with bipolar I disorder or bipolar II disorder compared to controls;</i>	
Bipolar I disorder: 45 studies, N < 5,024, d = 0.22, 95%CI -0.02 to 0.47, p not reported, I ² = 90%	
Bipolar II disorder: 22 studies, N < 3,421, d = 0.39, 95%CI -0.13 to 0.92, p not reported, I ² = 95%	

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<i>No differences in attention between bipolar I disorder and bipolar II disorder; 19 studies, N not reported, $d = 0.02$, 95%CI -0.35 to 0.40, p not reported, $I^2 = 81\%$</i>	
Consistency in results	Inconsistent
Precision in results	Precise, apart from bipolar II disorder vs. controls.
Directness of results	Direct

<i>Elias LR, Miskowiak KW, Vale AM, Kohler CA, Kjaerstad HL, Stubbs B, Kessing LV, Vieta E, Maes M, Goldstein BI, Carvalho AF</i>	
Cognitive Impairment in Euthymic Pediatric Bipolar Disorder: A Systematic Review and Meta-Analysis	
Journal of the American Academy of Child & Adolescent Psychiatry 2017; 56: 286-96	
View review abstract online	
Comparison	Attention in euthymic youth with bipolar disorder vs. controls of similar age (mean 13 years) and IQ (mean 104).
Summary of evidence	Moderate to high quality evidence (large sample, inconsistent, precise, direct) suggests no differences in attention/vigilance.
Attention/vigilance	
<i>No significant differences were found for attention/vigilance; 12 studies, N = 603, $d = 0.18$, 95%CI -0.06 to 0.43, $p = 0.144$, $I^2 = 50\%$, $p < 0.05$</i>	
Consistency in results	Inconsistent
Precision in results	Precise
Directness of results	Direct

<i>Samame C, Martino DJ, Strejilevich SA</i>	
A quantitative review of neurocognition in euthymic late-life bipolar disorder	

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<p>Bipolar Disorders 2013; 15: 633-44 View review abstract online</p>	
Comparison	Attention in older people with bipolar disorder vs. controls matched for age and years of education.
Summary of evidence	Moderate to high quality evidence (medium-sized samples, consistent, precise, direct) suggests a medium-sized effect of poorer attention in elderly people with bipolar disorder. Studies matched their samples for age and education, and subgroup analyses showed no between-study differences in results according to age and education.
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<p><i>Medium-sized, significant effects of poorer sustained attention in elderly people with bipolar disorder;</i></p> <p>5 studies, N = 368, $g = 0.61$, 95%CI 0.39 to 0.82, $p < 0.001$, $I^2 = 0\%$, $p = 0.82$</p> <p>Subgroup analyses showed no changes in the effect size according to age or years of education. The analysis remained significant when the analysis included only studies of patients in a depression phase ($g = 0.36$).</p>	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

<p><i>Samame C, Szmulewicz AG, Valerio MP, Martino DJ, Strejilevich SA</i></p> <p>Are major depression and bipolar disorder neuropsychologically distinct? A meta-analysis of comparative studies</p> <p>European Psychiatry 2017; 39: 17-26 View review abstract online</p>	
Comparison	Attention in people with bipolar disorder vs. people with major depression.
Summary of evidence	Moderate quality evidence (large samples, some inconsistencies and imprecision, direct) suggests no differences on tasks of attention.

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<i>There were no significant differences between groups;</i>	
<u>During euthymia</u>	
TMT-A: 4 studies, N = 333, $g = 0.00$, 95%CI -0.22 to 0.22, $p = 0.99$, $I^2 = 0\%$, $p = 0.45$	
TMT-B: 5 studies, N = 383, $g = -0.06$, 95%CI -0.55 to 0.43, $p = 0.82$, $I^2 = 78\%$, $p < 0.001$	
<u>During depression</u>	
TMT-A: 3 studies, N = 540, $g = 0.19$, 95%CI -0.58 to 0.97, $p = 0.49$, $I^2 = 87\%$, $p < 0.001$	
TMT-B: 3 studies, N = 540, $g = 0.65$, 95%CI -0.59 to 1.90, $p = 0.30$, $I^2 = 94\%$, $p < 0.001$	
Forward digit span: 3 studies, N = 680, $g = 0.07$, 95%CI -0.20 to 0.35, $p = 0.60$, $I^2 = 51\%$, $p = 0.13$	
Consistency in results	Inconsistent for TMT-A (depression) and TMT-B (euthymia and depression).
Precision in results	Imprecise for TMT-A (depression) and TMT-B (depression).
Directness of results	Direct

<p><i>Samame C, Martino DJ, Strejilevich SA</i></p> <p>Longitudinal course of cognitive deficits in bipolar disorder: a meta-analytic study</p> <p>Journal of Affective Disorders 2014; 164: 130-8</p> <p>View review abstract online</p>	
Comparison	Changes in attention over time in people with bipolar disorder.
Summary of evidence	Moderate quality evidence (small samples, consistent, precise, direct) suggests no changes in measures of attention over time (~3-5 years).
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<i>There were no significant changes over time;</i>	
TMT-A: 5 studies, N = 169, follow up = 4.87 years, $d = 0.04$, 95%CI -0.18 to 0.25, $p = 0.75$, $I^2 = 0\%$, $p = 0.55$	
TMT-B: 5 studies, N = 169, follow up = 4.87 years, $d = -0.19$, 95%CI -0.47 to 0.10, $p = 0.19$, $I^2 = 37\%$, $p = 0.18$	
Stroop (interference): 4 studies, N = 131, follow up = 4.90 years, $d = 0.01$, 95%CI -0.26 to 0.29, $p =$	

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0.93, $I^2 = 0\%$, $p = 0.64$	
CPT: 3 studies, N = 102, follow up = 2.68 years, $d = 0.01$, 95%CI -0.27 to 0.28, $p = 0.96$, $I^2 = 0\%$, $p = 0.56$	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Direct

Explanation of acronyms

CI = confidence interval, CPT = continuous performance test, d = Cohen’s d and g = Hedges’s g 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, Q = test for heterogeneity, r = correlation coefficient, TMT = trail-making test

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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 small¹⁵.

† 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 effect¹⁵.

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 ¹⁶. InOR stands for logarithmic OR where a InOR 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 unforeseen 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 formula¹⁵;

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

§ 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 relaxed¹⁷.

|| 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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