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

**Running Title:** Cognition in schizoaffective disorder

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## Abstract

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*Background:* The nature and degree of cognitive impairments in schizoaffective disorder is not well established. The aim of this meta-analysis was to characterise cognitive functioning in schizoaffective disorder and compare it with cognition in schizophrenia and bipolar disorder. Schizoaffective disorder was considered both as a single category and as its two diagnostic subtypes, bipolar and depressive disorder.

*Methods:* Following a thorough literature search (468 records identified), we included 31 studies with a total of 1685 participants with schizoaffective disorder, 3357 with schizophrenia and 1095 with bipolar disorder. Meta-analyses were conducted for seven cognitive variables comparing performance between participants with schizoaffective disorder and schizophrenia, and between schizoaffective disorder and bipolar disorder.

*Results:* Participants with schizoaffective disorder performed worse than those with bipolar disorder ( $g=-0.30$ ) and better than those with schizophrenia ( $g=0.17$ ). Meta-analyses of the subtypes of schizoaffective disorder showed cognitive impairments in participants with the depressive subtype are closer in severity to those seen in participants with schizophrenia ( $g=0.08$ ), whereas those with the bipolar subtype were more impaired than those with bipolar disorder ( $g=-0.23$ ) and less impaired than those with schizophrenia ( $g=0.29$ ). Participants with the depressive subtype had worse performance than those with the bipolar subtype but this was not significant ( $g=0.25$ ,  $p=0.05$ ).

*Conclusion:* Cognitive impairments increase in severity from bipolar disorder to schizoaffective disorder to schizophrenia. Differences between the subtypes of schizoaffective disorder suggest combining the subtypes of schizoaffective disorder may obscure a study's results and hamper efforts to understand the relationship between this disorder and schizophrenia or bipolar disorder.

*Key words:* Schizoaffective disorder / subtypes / review / memory / attention

# 1 Introduction

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2 Schizophrenia and bipolar disorder have traditionally been considered to be discrete  
3 categories in diagnostic classification. In contrast studies examining clinical features,  
4 genetic risk and neuroimaging data suggest there are overlaps between these  
5 disorders (Craddock & Owen, 2010; Ivleva et al., 2013; Keshavan et al., 2011;  
6 Ruderfer et al., 2018). The intermediate diagnosis, “schizoaffective disorder” was  
7 introduced due to the observation that some patients exhibit symptoms of  
8 schizophrenia and mood disturbance (Jäger, Haack, Becker, & Frasch, 2011).

9 Schizoaffective disorder can be separated into two distinct subtypes: depressive and  
10 bipolar. However, the relationship between schizoaffective disorder, including the  
11 two subtypes, and schizophrenia or bipolar disorder remains unclear. Investigating  
12 the nature and degree of the cognitive impairments associated with schizoaffective  
13 disorder may further elucidate the relationship between these psychotic disorders.

14 It is well established that a broad range of cognitive abilities are impaired in a large  
15 number of patients with schizophrenia (Fatouros-Bergman, Cervenka, Flyckt, Edman,  
16 & Farde, 2014; Fioravanti, Carlone, Vitale, Cinti, & Clare, 2005; Heinrichs & Zakzanis,  
17 1998). Cognitive impairments are also present in patients with schizoaffective  
18 disorder and bipolar disorder, albeit milder than in schizophrenia (Emre Bora, Yucel,  
19 & Pantelis, 2009; Krabbendam, Arts, van Os, & Aleman, 2005; Stefanopoulou et al.,  
20 2009). These differences are not consistent across cognitive domains. Bora et al.  
21 (Emre Bora et al., 2009) reported differences between participants with  
22 schizophrenia and affective psychosis (schizoaffective disorder and bipolar disorder)  
23 in verbal memory, IQ, verbal working memory and executive function but no

24 differences in visual memory, attention or spatial working memory tests in their  
25 meta-analysis of twelve cognitive abilities.

26 Meta-analyses comparing cognitive performance between schizophrenia and  
27 affective psychosis have detected heterogeneity of effect sizes between studies  
28 (Emre Bora et al., 2009; Krabbendam et al., 2005). More recent reviews have  
29 attempted to reduce this heterogeneity by examining specific diagnoses and  
30 subgroups (E. Bora, Yucel, Fornito, Berk, & Pantelis, 2008; Kuswanto et al., 2016; K.  
31 Lewandowski, Cohen, & Öngur, 2011; Madre et al., 2016). These reviews have  
32 concluded that participants with schizophrenia, particularly those with prominent  
33 negative symptoms, exhibit the most severe cognitive deficits (E. Bora et al., 2008;  
34 Kuswanto et al., 2016; K. Lewandowski et al., 2011). Participants with bipolar  
35 disorder and no history of psychosis have the least severe cognitive deficits (E. Bora  
36 et al., 2008; Kuswanto et al., 2016; K. Lewandowski et al., 2011). There is also  
37 evidence that participants with bipolar disorder – type II have better cognitive  
38 functioning than participants with bipolar disorder – type I (Simonsen et al., 2008;  
39 Torrent et al., 2006). The cognitive performance of participants with either bipolar  
40 disorder and psychosis or schizoaffective disorder appears to be intermediate  
41 between bipolar disorder without psychosis and schizophrenia (E. Bora et al., 2008;  
42 Kuswanto et al., 2016). Bora et al. (E. Bora et al., 2008) concluded that participants  
43 who were experiencing psychotic symptoms during assessment exhibited similar  
44 cognitive impairments irrespective of diagnosis. However, Madre et al. (Madre et al.,  
45 2016) suggest that the degree of cognitive impairments in schizoaffective disorder is  
46 closer to that of schizophrenia than bipolar disorder and schizoaffective disorder  
47 may represent a subtype of schizophrenia.

48 To date, reviews examining the subtypes of disorders have conducted narrative  
49 synthesis of the studies but there have been no attempts to aggregate this existing  
50 data into a meta-analysis. To our knowledge, there have been no meta-analyses  
51 comparing cognitive function between schizoaffective disorder and bipolar disorder  
52 or comparing the subtypes of schizoaffective disorder. We feel this is an important  
53 consideration as there is evidence to suggest that the depressive subtype of  
54 schizoaffective disorder may be associated with cognitive impairment closer to that  
55 of schizophrenia, whilst those with the bipolar subtype are less impaired (Hill et al.,  
56 2013; Lynham et al., 2018). This suggests that the proportion of each subtype  
57 included in schizoaffective disorder samples could influence study results.

58 Our aim was to conduct meta-analyses to examine cognitive performance across the  
59 bipolar-schizophrenia diagnostic spectrum. Studies that compared the subtypes of  
60 schizoaffective disorder to schizophrenia and bipolar disorder were also reviewed.

61 Our hypothesis was that cognitive impairments in schizoaffective disorder would be  
62 intermediate between those observed in bipolar disorder and schizophrenia. We  
63 further hypothesised that the depressive subtype of schizoaffective disorder would  
64 be associated with more severe cognitive impairments similar to schizophrenia,  
65 whilst impairments in the bipolar subtype would be less severe than those of  
66 schizophrenia but more impaired than those of bipolar disorder.

## 67 **Methods**

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### 68 **Study selection**

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70 This review was conducted following guidelines from the Preferred Reporting Items  
71 for Systematic Reviews and Meta-Analyses (PRISMA) (Moher, Liberati, Tetzlaff, &

72 Altman, 2009). We conducted searches for articles published between January 1980  
73 and February 2019 in PubMed, PsycINFO, Web of Science and EMBASE. The  
74 keywords, “schizophrenia”, “schizoaffective” and “bipolar” combined with  
75 “cogniti\*”, “neurocogniti\*” and “neuropsycholog\*” were used. The latter terms  
76 were also replaced with keywords that describe cognitive domains (memory,  
77 attention and executive function). The bibliographies of published articles were also  
78 reviewed.

79 The inclusion criteria included all full text publications that:

- 80 1. Directly compared participants with schizoaffective disorder to those with  
81 schizophrenia, bipolar disorder or both disorders but did not combine  
82 different diagnoses into a single group (e.g. affective psychosis).
- 83 2. Included adults (aged 16 years or over) diagnosed using versions of DSM, ICD  
84 or Research Diagnostic Criteria (RDC).
- 85 3. Included published assessments of cognition for the following domains:  
86 executive function, speed of processing, working memory, immediate verbal  
87 learning, immediate visuospatial learning or verbal fluency.
- 88 4. Reported independent data. When studies with overlapping samples were  
89 identified and both met inclusion criteria, the study with the largest sample  
90 was selected.

91 Recorded variables were:

- 92 1. Name of the first author and year of publication
- 93 2. Number of participants in each diagnostic group and proportion of subtypes  
94 for schizoaffective disorder
- 95 3. Sample characteristics (inpatients or outpatients, diagnostic criteria used)  
96 and status of patients (acute, stabilised, in remission), where defined



97 4. Cognitive test or battery results.

98 Authors were contacted for missing data.

99 **Neuropsychological variables**

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100 We set an a priori primary study outcome of a general cognitive performance  
101 measure that allowed comparisons across studies. We calculated this composite  
102 cognition effect size and its 95% confidence intervals using the mean and standard  
103 error of the effect sizes of the individual tests or domains. This included all tests  
104 reported in each paper in order to maximise the number of studies included.  
105 Composite scores were only calculated for studies with three or more tests available,  
106 as has been done in previous studies (Lencz et al., 2013).

107 In addition to general cognitive function, we selected domains based on the  
108 Measurement in Assessment and Treatment Research to Improve Cognition in  
109 Schizophrenia (MATRICS) initiative (Nuechterlein et al., 2004), as we have done in  
110 our previous work (Niarchou et al., 2013). Tasks were assigned to domains based on  
111 the MATRICS and previous reviews (Emre Bora et al., 2009; Kuswanto et al., 2016).  
112 The domains included were verbal learning, visuospatial learning, executive function,  
113 speed of processing, verbal fluency and working memory. The tasks included in each  
114 domain can be found in supplementary table S1. If a study included more than one  
115 task for a single domain, the effect sizes were averaged to create a single domain  
116 score. For tasks with multiple outcome measures, the most common outcome  
117 measure used across the studies was included.

## 118 **Statistical analyses**

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119 Meta-analyses were conducted to compare general cognitive performance and  
120 domain-specific cognition between the following diagnoses:

- 121 1. Schizoaffective disorder and schizophrenia (N=22)
- 122 2. Schizoaffective disorder and bipolar disorder (N=10)
- 123 3. Schizoaffective disorder and bipolar disorder with psychosis (N=4)
- 124 4. Schizoaffective disorder and bipolar disorder without psychosis (N=3)
- 125 5. Schizoaffective disorder – depressive type and schizophrenia (N=4)
- 126 6. Schizoaffective disorder – depressive type and bipolar disorder (N=3)
- 127 7. Schizoaffective disorder – bipolar type and schizophrenia (N=3)
- 128 8. Schizoaffective disorder – bipolar type and bipolar disorder (N=4)
- 129 9. Schizoaffective disorder – bipolar type and schizoaffective disorder –  
130 depressive type (N=2)

131 Effect sizes were calculated for each pair of comparisons using the formulas  
132 described by Rosnow and Rosenthal (Rosnow & Rosenthal, 1996) and Rosnow,  
133 Rosenthal and Rubin (Rosnow, Rosenthal, & Rubin, 2000). We used Hedge’s  
134 correction for bias due to uneven group sizes to calculate the pooled standard  
135 deviation (Hedges & Olkin, 1985). All effect sizes were calculated such that a positive  
136 effect size would indicate that the schizoaffective disorder group had performed  
137 better than the comparison group.

138 Meta-analyses were conducted using the package, “meta” in R v3.3.1. A random  
139 effects model was used (DerSimonian-Laird estimate (DerSimonian & Laird, 1986)).  
140 Effect sizes were weighted using the inverse variance method. Homogeneity of the

141 effect sizes was tested using the Q-test. Funnel plots and Egger’s test were used to  
142 assess reporting bias.

143 Meta-regression analyses were conducted to estimate the moderating effects of age,  
144 sex, years in education, age of onset, illness duration, current antipsychotic  
145 medication use, current psychotic symptoms, current depressive symptoms, current  
146 negative symptoms and current manic symptoms on the composite cognition  
147 findings. Meta-regression analyses were performed with a random effects model  
148 using the restricted-information maximum likelihood method in R using the package,  
149 “metafor”.

150 A sensitivity analysis was conducted by repeating the meta-analysis comparing  
151 bipolar disorder and schizoaffective disorder excluding papers that included bipolar  
152 disorder - type II in their sample.

153

## 154 **Results**

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### 155 156 **Retrieved studies**

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157 A total of 468 records were identified from the initial searches and the abstracts  
158 screened for inclusion. Initially, 419 studies were excluded as either duplicates or not  
159 meeting inclusion criteria. A further 18 articles were excluded after examination of  
160 the full texts, mainly because these studies had combined diagnostic groups and  
161 thus we were unable to calculate separate effect sizes. One study was excluded  
162 because summary statistics or effect sizes were not available. This resulted in 31  
163 studies being included in the meta-analysis. In total, there were 1685 participants  
164 with schizoaffective disorder, 3357 participants with schizophrenia and 1095  
165 participants with bipolar disorder. Figure 1 shows the PRISMA flowchart illustrating  
166 the process of filtering potential studies. Full details of the final studies included can  
167 be found in supplementary table S2.

### 168 **Schizophrenia and schizoaffective disorder**

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169 Composite cognition effect sizes were calculated for 22 studies comparing  
170 schizoaffective disorder (n=1166) and schizophrenia (n=2851). Participants with  
171 schizoaffective disorder performed better than participants with schizophrenia  
172 based on composite cognition scores ( $g=0.17$ ,  $p<0.0001$ , see Figure 2). Effect size  
173 distributions were homogeneous ( $T^2=0.002$ ;  $Q=22.64$ ,  $p=0.36$ ) and there was no  
174 evidence of publication bias (Egger: bias = -0.23). Meta-regression analyses were  
175 conducted to investigate the influence of nine variables: age, sex, years in education,  
176 age of onset, duration of illness, antipsychotic use, psychotic, depressive and

177 negative symptoms. Meta-regression analyses were not significant for any of the  
178 variables examined (see supplementary table S3).

179 In analyses examining individual cognitive domains, the schizoaffective group  
180 outperformed the schizophrenia group in verbal learning ( $g=0.24$ ), speed of  
181 processing ( $g=0.18$ ), visuospatial learning ( $g=0.20$ ), verbal fluency ( $g=0.14$ ) and  
182 working memory ( $g=0.09$ ), although there was evidence of heterogeneity in the  
183 domains of verbal learning, executive function and speed of processing (see  
184 supplementary table S4).

185 The meta-analyses were repeated for the separate subtypes of schizoaffective  
186 disorder: schizoaffective bipolar type and schizoaffective depressive type (see Table  
187 1 for results). There was no significant difference between participants with  
188 schizophrenia and participants with schizoaffective disorder – depressive type  
189 ( $g=0.08$ ,  $p=0.35$ ). Participants with schizoaffective disorder – bipolar type  
190 outperformed participants with schizophrenia ( $g=0.29$ ,  $p=0.0003$ ). The results of the  
191 Q-test and Egger’s test indicated that there was little evidence of heterogeneity or  
192 publication bias, but these tests have low power when there is only a small number  
193 of studies included.

#### 194 **Bipolar disorder and schizoaffective disorder**

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195 Composite cognition effect sizes were calculated for 10 studies comparing  
196 schizoaffective disorder ( $n=732$ ) and bipolar disorder ( $n=946$ ). Participants with  
197 schizoaffective disorder performed worse than participants with bipolar disorder  
198 ( $g=-0.30$ ,  $p<0.0001$ , see Figure 3). Effect size distributions were homogeneous  
199 ( $T^2<0.0001$ ;  $Q=7.75$ ,  $p=0.56$ ) and there was no evidence of publication bias (Egger:

200 bias = 0.99). These results did not change when the analysis was repeated including  
201 participants with bipolar disorder – type I only ( $g=-0.30$ ,  $p<0.0001$ ). Participants with  
202 schizoaffective disorder performed worse than participants with bipolar disorder and  
203 psychosis ( $g=-0.39$ ,  $p=0.0002$ ), and participants with bipolar disorder without a  
204 history of psychosis ( $g=-0.47$ ,  $p=0.001$ ). Meta-regression analyses were conducted to  
205 investigate the influence of eight variables: age, sex, duration of illness, antipsychotic  
206 use, psychotic, depressive, negative and manic symptoms. There was insufficient  
207 data to examine the influence of age of onset and years in education for studies  
208 comparing bipolar disorder and schizoaffective disorder. Meta-regression analyses  
209 were not significant for any of the variables examined (see supplementary table S3).

210 In analyses examining individual cognitive domains, performance in the  
211 schizoaffective group was worse than bipolar disorder in verbal learning ( $g=-0.42$ ),  
212 executive function ( $g=-0.36$ ), speed of processing ( $g=-0.35$ ), verbal fluency ( $g=-0.32$ )  
213 and working memory ( $g=-0.30$ , see supplementary table S4). Data comparing  
214 visuospatial learning between bipolar disorder and schizoaffective disorder were not  
215 available. There was evidence of heterogeneity in the effect sizes for speed of  
216 processing ( $Q=13.45$ ,  $p=0.04$ ) and verbal learning ( $Q=13.41$ ,  $p=0.02$ ).

217 The meta-analyses were repeated for the separate subtypes of schizoaffective  
218 disorder: schizoaffective bipolar type and schizoaffective depressive type (see Table  
219 1 for results). The schizoaffective bipolar group had lower overall cognitive scores  
220 than bipolar disorder ( $g=-0.23$ ,  $p=0.003$ ). The schizoaffective depressive group were  
221 more impaired than those with bipolar disorder ( $g=-0.47$ ,  $p<0.0001$ ). The results of  
222 the Q-test and Egger's test indicated that there was little evidence of heterogeneity

223 or publication bias, but these tests have low power when there is only a small  
224 number of studies included.

### 225 **Subtypes of schizoaffective disorder**

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226 Only two studies reported separate cognitive data for both subtypes of  
227 schizoaffective disorder, bipolar (N=186) and depressive (N=167). Participants with  
228 the depressive subtype of schizoaffective disorder had worse performance than  
229 those with the bipolar subtype but this difference was not significant ( $g=0.25$ ,  
230  $p=0.05$ ). Effect size distributions were homogeneous ( $T^2=0.008$ ;  $Q=1.31$ ,  $p=0.25$ ).  
231 Egger's bias cannot be calculated for two studies.

### 232 **Discussion**

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233 The aim of this meta-analysis was to compare cognitive outcomes of schizoaffective  
234 disorder with schizophrenia and bipolar disorder. This is the first meta-analysis to  
235 compare cognitive performance of participants with schizoaffective disorder and  
236 bipolar disorder. It is also the first review that has examined whether the subtypes of  
237 schizoaffective disorder differ in cognitive outcomes compared to schizophrenia and  
238 bipolar disorder. Cognitive performance of participants with schizoaffective disorder  
239 was intermediate between those with bipolar disorder and schizophrenia. Meta-  
240 analyses of the subtypes of schizoaffective disorder indicated that participants with  
241 the depressive subtype had cognitive impairments closer in severity to those seen in  
242 participants with schizophrenia, whereas those with the bipolar subtype were more  
243 impaired than participants with bipolar disorder and less impaired than those with  
244 schizophrenia (see Figure 4). Participants with the depressive subtype had worse  
245 cognitive performance than those with the bipolar subtype but this was not

246 significant and only two studies had reported separate cognitive data for both  
247 subtypes.

### 248 **Schizoaffective disorder and bipolar disorder**

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249 The schizoaffective disorder group exhibited worse performance across all cognitive  
250 domains compared to the bipolar disorder group. This supports the conclusions of a  
251 review by Madre et al. (Madre et al., 2016) who suggested that cognitive  
252 impairments are more severe in schizoaffective disorder than in bipolar disorder.  
253 Other reviews have concluded that bipolar disorder and psychosis is associated with  
254 similar cognitive impairments to those seen in schizoaffective disorder (E. Bora et al.,  
255 2008), whilst participants with bipolar disorder and no history of psychosis have less  
256 severe deficits (E. Bora et al., 2008; Kuswanto et al., 2016; K. Lewandowski et al.,  
257 2011). We found evidence that both subtypes of bipolar disorder (with and without  
258 history of psychosis) had less severe impairments than schizoaffective disorder,  
259 although a larger magnitude of effect size was found between schizoaffective  
260 disorder and bipolar disorder without psychosis than the difference between  
261 schizoaffective disorder and bipolar disorder with psychosis. Our results expand on  
262 previous reviews by showing that mania within schizoaffective disorder is associated  
263 with less impaired cognition, compared to participants with schizoaffective disorder  
264 – depressive type and schizophrenia. Taken together, these results suggest that  
265 there is not a simple dichotomy in cognitive function between those with a history of  
266 psychosis and those without. The reasons why participants with a diagnosis of a  
267 manic disorder are less cognitively impaired than participants with schizophrenia are  
268 unclear but could include differences in illness course (episodic or chronic), symptom  
269 profiles, age of onset, medication or underlying psychopathology. In their meta-



270 analysis comparing cognition between schizophrenia and bipolar disorder, Bora et al.  
271 (Emre Bora et al., 2009) reported that variability in the magnitude of the effect sizes  
272 between studies was driven by the percentage of males, severity of negative  
273 symptoms and age of onset of the schizophrenia samples included, and these factors  
274 may also impact performance in schizoaffective disorder. There is some evidence  
275 that current mood symptoms, particularly depressive symptoms, are associated with  
276 greater impairments in executive function and verbal fluency (Chaves et al., 2011;  
277 Frangou, Donaldson, Hadjulis, Landau, & Goldstein, 2005). However, we did not find  
278 any moderating effects of current depressive, psychotic, manic or negative  
279 symptoms in these analyses.

280 Bipolar disorder – type I has been shown to be associated with more widespread  
281 cognitive impairments than type II (E. Bora, Yücel, Pantelis, & Berk, 2011). The  
282 results of a sensitivity analysis including type I only was comparable to the meta-  
283 analysis including both subtypes. However, it was not possible to compare bipolar  
284 disorder – type II and schizoaffective disorder, as only one study reported separate  
285 data for type II.

## 286 **Schizoaffective disorder and schizophrenia**

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287 Participants with schizoaffective disorder were less cognitively impaired than  
288 participants with schizophrenia. This is consistent with the findings of an earlier  
289 meta-analysis (Emre Bora et al., 2009). The effect size reported in the current study  
290 ( $g=0.17$ ) fell within the range of effect sizes reported by the earlier meta-analysis  
291 ( $d=0.08-0.32$ ). The difference between schizoaffective disorder and schizophrenia  
292 was smaller than the effect size of the schizoaffective disorder and bipolar disorder

293 analysis ( $g=-0.30$ ). This is consistent with the conclusions drawn in the review by  
294 Madre et al. (Madre et al., 2016), which suggested that the degree of cognitive  
295 impairments in schizoaffective disorder is closer to that of schizophrenia than bipolar  
296 disorder.

297 There were inconsistencies between the results of the individual studies, with  
298 approximately half of the studies reporting greater impairment in the schizophrenia  
299 group than the schizoaffective disorder group and the remaining studies reporting  
300 no differences. There are a number of factors that may account for these  
301 inconsistent findings, including differences in cognitive assessments, the recruitment  
302 of acutely unwell versus euthymic patients, and the inclusion of subtypes of  
303 schizophrenia and schizoaffective disorder. Studies included in this meta-analysis  
304 have reported that the presence of negative symptoms or the inclusion of  
305 participants with non-paranoid subtypes of schizophrenia are associated with more  
306 severe impairments (Bornstein et al., 1990; Goldstein, Shemansky, & Allen, 2005;  
307 Savage, Jackson, & Sourathathone, 2003; Torniainen et al., 2012). In addition, we  
308 found evidence that the subtypes of schizoaffective disorder may be associated with  
309 differing levels of cognitive impairment (Hill et al., 2013; Lynham et al., 2018)  
310 (discussed further in the next section). However, we did not find any moderating  
311 effects of age, sex, age of onset, duration of illness, years in education, psychotic,  
312 depressive or negative symptoms. In conclusion, the proportion of participants with  
313 each subtype of schizoaffective disorder or schizophrenia may influence the effect  
314 sizes in comparisons of cognitive function between schizophrenia and schizoaffective  
315 disorder.

## 316 **Cognition across the three disorders**

---

317 It has been hypothesised that schizoaffective disorder may represent the midpoint in  
318 a bipolar-schizophrenia diagnostic spectrum (Crow, 1990). This spectrum ranges  
319 from bipolar disorder without psychosis at one end and schizophrenia without  
320 affective symptoms at the other with patients with features of both disorders falling  
321 at some point in the middle (Craddock & Owen, 2005; Crow, 1990; Owen, 2014).  
322 Support for a dimensional approach comes from research showing overlap in the  
323 symptom profiles of these disorders (Keshavan et al., 2011), as well as evidence that  
324 the functional outcome of schizoaffective disorder is poorer than bipolar disorder  
325 but better than schizophrenia (Benabarre et al., 2001; Harrow, Grossman, Herbener,  
326 & Davies, 2000). Our finding that the degree of cognitive impairment increases from  
327 bipolar disorder to schizoaffective disorder to schizophrenia is consistent with this  
328 view.

329 In our analyses of individual cognitive domains, participants with schizoaffective  
330 disorder were more impaired across all domains compared to participants with  
331 bipolar disorder. Effect sizes were smaller in comparisons between schizoaffective  
332 disorder and schizophrenia, but the most significant differences were observed for  
333 verbal learning ( $g=0.24$ ) and speed of processing ( $g=0.18$ ). Comparable effect sizes  
334 were reported in an earlier meta-analysis (Emre Bora et al., 2009), which found the  
335 schizophrenia group were more impaired than the schizoaffective disorder group on  
336 verbal memory ( $d=0.23$ ), Wisconsin Card Sorting Test ( $d=0.21$ ) and processing speed  
337 ( $d=0.24$ ). This is an interesting finding as previous studies have shown that most of  
338 the impairments in specific domains seen in participants with schizophrenia can be  
339 accounted for by a general intelligence factor ('g') but 'g' does not fully account for

340 deficits in processing speed and verbal learning (Dickinson, Iannone, Wilk, & Gold,  
341 2004; Dickinson, Ragland, Gold, & Gur, 2008). This suggests that these abilities may  
342 be disproportionately affected in patients with schizophrenia and may differentiate  
343 them from participants with schizoaffective disorder.

344 Few studies reported the proportion of subtypes of schizoaffective disorder in their  
345 sample. Therefore, it is difficult to draw any firm conclusions about differences in  
346 cognitive performance between the subtypes. In the subgroup analysis, no  
347 difference in cognitive performance was detected between participants with the  
348 depressive subtype and schizophrenia, although performance was marginally better  
349 in the schizoaffective disorder - depressive type group. A larger effect size was  
350 observed between the bipolar subtype and schizophrenia. Both subtypes were more  
351 impaired than bipolar disorder. These results suggest that the depressive subtype of  
352 schizoaffective disorder may have more severe cognitive impairments than those  
353 seen in the bipolar subtype and more closely resemble that of schizophrenia. Whilst  
354 there was some evidence of this in our comparison of the subtypes, this difference  
355 was not significant and should be interpreted with caution given that only two  
356 studies had data available.

### 357 **Limitations**

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358 Several limitations of this meta-analysis should be noted. A small number of studies  
359 specified the subtypes of schizoaffective disorder and only two studies contained  
360 disaggregated data on both subtypes. Therefore, the results for the subtypes should  
361 be interpreted with caution. The studies included in this review employed different  
362 measures of cognition, which may explain the heterogeneity in the distribution of

363 effect sizes for some domains. However, there was little evidence of heterogeneity  
364 in the analyses of composite cognition scores. There were also differences in the  
365 inclusion of stabilised and symptomatic participants across studies and few included  
366 a definition of remission. It has been argued that cognitive impairment may be  
367 affected by illness state at the time of assessment and studies of inpatients included  
368 in this meta-analysis reported no differences in cognitive performance between  
369 patient groups (Amann et al., 2012; K. E. Lewandowski, Cohen, Keshavan, & Öngür,  
370 2011; Szoke et al., 2008). Most studies included in this analysis recruited participants  
371 from outpatient clinics and therefore our results may not be generalizable to acutely  
372 unwell participants.

373 This meta-analysis included studies from a wide range of countries and thus their  
374 methodologies differed on diagnostic criteria and cognitive assessments (both type  
375 and language). The use of different diagnostic criteria is particularly relevant in this  
376 meta-analysis, as criteria for schizoaffective disorder varies considerably between  
377 the Diagnostic and Statistical Manual (DSM), International Classification of Diseases  
378 (ICD) and Research Diagnostic Criteria (RDC). The majority of the studies (N=27) used  
379 DSM criteria so the diagnosis of schizoaffective disorder relied on mood symptoms  
380 being present for a substantial proportion of the total illness duration, with a period  
381 of at least two weeks of psychosis in the absence of mood. In contrast, ICD (utilised  
382 by one study) places an emphasis on first rank symptoms of schizophrenia for the  
383 diagnosis of schizoaffective disorder. Vollmer-Larsen et al. (Vollmer-Larsen,  
384 Jacobsen, Hemmingsen, & Parnas, 2006) demonstrated that using ICD-10 and DSM-  
385 IV to diagnose schizoaffective disorder results in a different set of patients. Four  
386 studies defined schizoaffective disorder according to the RDC. Schizoaffective

387 disorder in RDC includes a broad range of patients including those with brief  
388 psychotic symptoms and chronic mood symptoms, and the converse (Spitzer,  
389 Endicott, & Robins, 1978). Thus, participants diagnosed with RDC schizoaffective  
390 disorder are a broad, heterogeneous group. The results of this meta-analysis are  
391 most generalizable to patients diagnosed according to the DSM and the results of  
392 studies using ICD or RDC may differ from those presented here.

### 393 **Conclusions**

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394 Based on this review, we make several recommendations for future research.  
395 Studies should report the clinical characteristics of their sample, including patient  
396 status (with defined remission criteria), measures of mood, psychosis and negative  
397 symptoms, and classes and doses of psychiatric medication. The results of our  
398 analyses separating the subtypes of schizoaffective disorder have important  
399 implications for diagnostic classification and highlight the importance of considering  
400 heterogeneity within disorders. Studies that simply combine the subtypes of  
401 schizoaffective disorder may produce conflicting results and hamper efforts to  
402 understand the relationship between this disorder and schizophrenia or bipolar  
403 disorder. Given the heterogeneity of cognitive performance within diagnoses and  
404 the overlap in clinical features and underlying biology between disorders, a  
405 dimensional approach to measuring psychopathology (such as the National Institute  
406 for Mental Health's Research Domain Criteria (T. Insel et al., 2010; T. R. Insel, 2014;  
407 Morris & Cuthbert, 2012)) may better inform investigations of the underlying  
408 aetiology of cognitive impairments in psychotic and mood disorders.

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## **Conflicts of interest**

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None

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## Figure Legends

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### **Figure 1 PRISMA flowchart illustrating the methodological process of filtering potential studies**

The records excluded at the screening phase (n=250) included 25 reviews and meta-analyses, 93 studies that compared schizophrenia and bipolar disorder but not schizoaffective disorder and 132 studies that did not fit the aims of this reviews. Full text articles were excluded due to combining diagnoses (n=10), children or adolescent participants (n=2), studies with unsuitable cognitive assessments (n=3), studies reported proportion of participants impaired or not impaired (n=2) or data was not available (n=1).

### **Figure 2 Forest plot of individual and pooled random effect estimates of mean differences between schizophrenia and schizoaffective disorder**

Positive effect sizes indicate better performance in the schizoaffective disorder group.

### **Figure 3 Forest plot of individual and pooled random effect estimates of mean differences between schizoaffective disorder and bipolar disorder**

Positive effect sizes indicate better performance in the schizoaffective disorder group.

### **Figure 4 Cognitive performance across the bipolar-schizophrenia diagnostic spectrum**

**Table S1: Tasks included in each domain**

<b>Verbal Learning</b>	<b>Visuospatial Learning</b>	<b>Executive Function</b>	<b>Speed of Processing</b>	<b>Verbal Fluency</b>	<b>Working Memory</b>
BACS: List Learning	BVMT-R	CANTAB: Stockings of Cambridge	BACS: Symbol Coding	BACS: Verbal Fluency	BACS: Digit sequencing
CVLT	BVRT				WAIS-R: Digit Span
HVLT-R	CANTAB: Paired Associates Learning	BACS: Tower of London	d2 Test	Category Fluency: Animal Naming	WAIS-III: Digit Span
RAVLT	WMS-R: Figural Memory	BADS: Composite Score	CNTRICS: Dot Probe Expectancy	COWAT	WAIS-R: Block Span
VLMT	WMS-III: Visual Memory	CCST (perseverative sorts)	SDMT	DKEFS: Verbal Fluency	WAIS-III: Block Span
WMS-III: Logical Memory		DKEFS: Colour-Word Interference	TMT A (time taken)	Letter Fluency	WAIS-III: Letter-Number Sequencing
		NAB: Mazes	WAIS-III: Symbol Search		WM-MA 2-back
		SCWT	WAIS-R: Digit Symbol Substitution		WMS-R: Digit Span
		TMT B (time taken)			WMS-R: Visual Span
		WAIS-R: Block Design			WMS-III: Letter-Number Sequencing
		WAIS-III: Matrix Reasoning			WMS-III: Spatial Span
		WCST (perseverative errors)			

*Abbreviations:* BACS, Brief Assessment of Cognition in Schizophrenia; BADS, Behavioural Assessment of the Dysexecutive Syndrome; BVMT-R, Brief Visuospatial Memory Test – Revised; BVRT, Benton Visual Retention Test; CANTAB, Cambridge Neuropsychological Test Automated Battery; CCST, California Card Sorting Test; CNTRICS, Cognitive Neuroscience Test Reliability and Clinical Applications for Schizophrenia; COWAT, Controlled Oral Word Association Test; CVLT, California Verbal Learning Test; D-KEFS, Delis-Kaplan Executive Function System; HVLT-R, Hopkins Verbal Learning Test – Revised; NAB: Neuropsychological Assessment Battery; RAVLT, Rey Auditory Verbal Learning Test; SCWT, Stroop Colour-Word Test; SDMT, Symbol Digits Modalities Test; TMT, Trail Making Test; VLMT, Verbal Learning & Retention Test; WAIS-III, Wechsler Adult Intelligence Scale - Third Edition; WAIS-R, Wechsler Adult Intelligence Scale – Revised Edition; WCST, Wisconsin Card Sorting Test; WM-MA, Working Memory – Mental Arithmetic Test; WMS-III, Wechsler Memory Scale – Third Edition; WMS-R, Wechsler Memory Scale – Revised Edition.

Table S2: Summary of studies included in meta-analysis

Study	Sample	Currently taking antipsychotics	Sample Characteristics	Neuropsychological Assessment	Hedge's g		
					SA vs. SZ	SA vs. BD	
<b>Amann et al.</b> <sup>1</sup>	26 SA (bipolar)	26/26 (100%)	Acutely unwell	WMS-III Verbal Memory	0.37	0.16	
	45 SZ	44/45 (98%)	inpatients	WMS-III Working Memory	0.02	0.05	
	51 BD	46/51 (90%)	DSM-IV	WMS-III Visual Memory	0.26	-0.07	
	65 HC		SA also met RDC	BADS Total	-0.12	0.12	
<b>Beatty et al.</b> <sup>2</sup>	11 SA		Outpatients	CCST free sorting (perseverative sorts)	0.26		
	10 SZ (3 paranoid, 7 undifferentiated)		DSM-III-R				
<b>Birindelli et al.</b> <sup>3</sup>	40 SA		Outpatients	CVLT (trials 1-5)	0.56		
	64 SZ		DSM-IV-TR	TMT A	0.08		
			In remission	TMT B	0.21		
				WCST (perseverative errors)	0.43		
<b>Bornstein et al.</b> <sup>4</sup>	18 SA		Primarily	WAIS-R Verbal IQ	0.29		
	55 SZ (28 paranoid, 27 non-paranoid)		outpatients	WAIS-R Performance IQ	0.11		
			DSM-III-R	HRB Category Test (no of errors)	0.11		
	52 HC				WCST (perseverative errors)	0.66	
					VCAT	0.90	
					Verbal Fluency	-0.26	
					Verbal WMS-R	0.42	
					Spatial WMS-R	-0.01	
					HRB TPT Time	0.24	
					HRB TPT Memory	-0.55	
					HRB TPT Location	0.47	
					HRB Speech Perception	0.22	
					HRB Seashore Rhythm	0.17	
			HRB TMT A	0.13			
			HRB TMT B	0.47			

Table S2 (cont.): Summary of studies included in meta-analysis

Study	Sample	Currently taking antipsychotics	Sample Characteristics	Neuropsychological Assessment	Hedge's g	
					SA vs. SZ	SA vs. BD
<b>Bornstein et al.</b> <sup>4</sup> <b>(cont.)</b>	18 SA 55 SZ (28 paranoid, 27 non-paranoid) 52 HC		Primarily outpatients DSM-III-R	HRB Finger Tap (right)	0.19	
				HRB Finger Tap (left)	0.34	
				HRB Grooved Peg (right)	0.40	
				HRB Grooved Peg (left)	0.05	
				HRB Finger Agnosia (right)	0.54	
				HRB Finger Agnosia (left)	0.35	
				HRB Graphesthesia (right)	0.42	
				HRB Graphesthesia (left)	0.29	
<b>Chen et al.</b> <sup>5</sup>	50 SA (41 bipolar, 9 depressive) 48 SZ 41 BD (all type I)	98%  100% 68%	Stable patients from general and psychiatric hospitals DSM-IV-TR	Verbal Memory	-0.11	-0.31
				Working Memory	-0.17	-0.22
				Motor Speed	0.57	-0.33
				Verbal Fluency	-0.09	-0.33
				Attention & Processing Speed	0.03	-0.52
				Executive Function	-0.04	-0.46
<b>DeRosse et al.</b> <sup>6</sup>	129 SA 595 SZ (224 with mood, 371 without mood) 269 BD (Type-I with psychosis)		Inpatients and outpatients DSM-IV	WAIS-R Digit Span	0.004	-0.27
				CVLT	0.33	-0.23
				COWAT	-0.02	-0.06
				Verbal Fluency: Animal Naming	0.08	-0.28
				TMT A	0.10	-0.08
				TMT B	0.04	-0.38
<b>Evans et al.</b> <sup>7</sup>	24 SA (depressive and bipolar subtypes) 115 SZ	20/24 (69%)  103/115 (67%)	Outpatients, including veterans DSM-III-R	Verbal Ability	-0.02	
				<i>Aphasia Screening Test</i>		
				<i>WAIS-R Vocabulary</i>		
				<i>Boston Naming Test</i>		
				<i>WAIS-R Similarities</i>		
				<i>Thurstone Written Fluency</i>		
				<i>COWAT (FAS)</i>		

Table S2 (cont.): Summary of studies included in meta-analysis

Study	Sample	Sample Characteristics	Neuropsychological Assessment	Hedge's g	
				SA vs. SZ	SA vs. BD
Evans et al. <sup>7</sup> (cont.)	24 SA (depressive and bipolar subtypes) 115 SZ	Outpatients, including veterans DSM-III-R	Psychomotor Speed	-0.16	
			<i>TMT A</i>		
			<i>WAIS-R Object Assembly</i>		
			<i>WAIS-R Digit Symbol</i>		
			<i>WAIS-R Block Design</i>		
			<i>TPT</i>		
			<i>Digit Vigilance Test (time)</i>		
			Abstraction / Cognitive Flexibility	-0.34	
			<i>Booklet Category Test</i>		
			<i>TMT B</i>		
			<i>WCST</i>		
			Attention	-0.18	
			<i>WAIS-R Digit Span</i>		
			<i>Digit Vigilance Test (errors)</i>		
Learning and Incidental Memory	-0.38				
<i>CVLT (trials 1-5)</i>					
<i>Figure Memory Test (learning)</i>					
<i>Story Memory Test (learning)</i>					
Retention	-0.32				
<i>CVLT (long delay recall)</i>					
<i>Figure Memory Test (delayed)</i>					
<i>Story Memory Test (delayed)</i>					
Motor	-0.07				
<i>Finger Tapping Test</i>					
<i>Grooved Pegboard Test</i>					
			<i>Hand dynamometer</i>		



Table S2 (cont.): Summary of studies included in meta-analysis

Study	Sample	Currently taking antipsychotics	Sample Characteristics	Neuropsychological Assessment	Hedge's g	
					SA vs. SZ	SA vs. BD
<b>Fiszdon et al.</b> <sup>8</sup>	73 SA 199 SZ		Outpatients DSM-IV	WCST (% conceptual level)	0.05	
				WAIS-III Digit Symbol	0.21	
				WAIS-III Digit Span	0.16	
				WMS-R Logical Memory I	0.34	
				HVLT-R	0.14	
				WMS-R Figural Memory	0.31	
<b>Gilvarry et al.</b> <sup>9</sup>	296 SA 223 SZ		Outpatients RDC	TMT A	0.02	
				TMT B	-0.17	
<b>Glahn et al.</b> <sup>10</sup>	15 SA (depressive) 15 SZ 26 BD (11 with history of psychosis, 15 without psychosis) 32 HC	100%	Outpatients DSM-IV Mixture of symptomatic and remitted patients	WAIS-III Forward Digit Span	0.20	-0.27
		100%		WAIS-III Backward Digit Span	-0.08	-0.38
		91% with psychosis, 13% without psychosis				
<b>Goldstein et al.</b> <sup>11</sup>	20 SA 63 SZ (29 undifferentiated, 20 paranoid, 14 residual)	100%	Male veterans Stabilised inpatients DSM-III-R	HRB Category Test	0.72	
		100%		HRB TPT	0.31	
				TMT B	0.56	
				WCST (errors)	0.14	
				WAIS-R Information	0.27	
				WAIS-R Digit Span	-0.11	
				WAIS-R Vocabulary	0.85	
				WAIS-R Arithmetic	0.77	
				WAIS-R Comprehension	1.05	
				WAIS-R Similarities	0.17	
				WAIS-R Picture Completion	0.55	
				WAIS-R Picture Arrangement	0.21	
				WAIS-R Block Design	0.42	

Table S2 (cont.): Summary of studies included in meta-analysis

Study	Sample	Currently taking antipsychotics	Sample Characteristics	Neuropsychological Assessment	Hedge's g	
					SA vs. SZ	SA vs. BD
<b>Goldstein et al.</b> <sup>11</sup> (cont.)	20 SA	100%	Male veterans	WAIS-R Object Assembly	0.23	
	63 SZ (29 undifferentiated, 20 paranoid, 14 residual)	100%	Stabilised inpatients DSM-III-R	WAIS-R Digit Symbol	0.35	
<b>Gooding &amp; Tallent</b> <sup>12</sup>	23 SA (19 bipolar, 4 depressive)	21/23 (91%)	Outpatients RDC	WCST (perseverative errors)	-0.18	
	34 SZ (15 paranoid, 12 residual, 6 undifferentiated, 1 disorganised) 30 HC	34/34 (100%)				
<b>Heinrichs et al.</b> <sup>13</sup>	48 SA 103 SZ 72 HC		Outpatients DSM-IV	WAIS-III Vocabulary	0.70	
				WAIS-III Matrix Reasoning	0.50	
				WAIS-III Letter-Number	0.53	
				WAIS-III Symbol Search	0.63	
				CVLT (trials 1-5)	0.65	
				COWAT	0.46	
				WRAT-3 Reading	0.44	
<b>Hill et al.</b> <sup>14</sup>	165 SA (55 depressive, 110 bipolar) 293 SZ 227 BD (all with history of psychosis) 295 HC	143/165 (87%) 264/293 (90%) 164/227 (72%)	Outpatients DSM-IV	BACS Verbal Memory	0.05	-0.37
				BACS Tower of London	0.38	-0.24
				BACS Symbol Coding	0.33	-0.17
				BACS Verbal Fluency	0.14	-0.32
				BACS Digit Sequencing	0.10	-0.37
<b>Leposavic et al.</b> <sup>15</sup>	30 SA 31 SZ (paranoid) 30 HC	100% 100%	Stabilised inpatients ICD-10	VITI Information	-0.23	
				VITI Digit Span	-0.31	
				VITI Vocabulary	-0.17	

Table S2 (cont.): Summary of studies included in meta-analysis

Study	Sample	Currently taking antipsychotics	Sample Characteristics	Neuropsychological Assessment	Hedge's g	
					SA vs. SZ	SA vs. BD
<b>Leposavic et al.</b> <sup>15</sup> <b>(cont.)</b>	30 SA	100%	Stabilised inpatients ICD-10	VITI Arithmetic	-0.65	
	31 SZ (paranoid)	100%		VITI Comprehension	-0.38	
	30 HC			VITI Similarities	-0.08	
				VITI Picture Completion	-0.19	
				VITI Picture Arrangement	-0.07	
				VITI Block Design	-0.90	
				VITI Object Assembly	-0.85	
				VITI Digit Symbol	-0.44	
				MMSE	-2.42	
				TMT A	0.16	
				TMT B	-0.22	
				HVOT	0.42	
				RCF (delayed recall)	-0.34	
		RAVLT (total words)	0.22			
		WCST (perseverative errors)	-0.77			
<b>Lewandowski et al.</b> <sup>16</sup>	29 SA (all bipolar type) 25 SZ 31 BD (all with history of psychosis) 20 HC		Stabilised inpatients and outpatients DSM-IV-TR	TMT B	0.69	-0.07
<b>Lynham et al.</b> <sup>17</sup>	188 SA (76 bipolar, 112 depressive)	77%	Stabilised outpatients DSM-IV	HVLT-R	0.27	-0.59
	558 SZ	86%		NAB: Mazes	-0.05	-0.51
	78 BD (68 type I & 10 type II / 59 with a history of psychosis & 19 without)	63%		BVMT-R	0.26	-0.49
				CPT-IP	0.23	-0.30
				TMT A	0.17	-0.50
		BACS: Symbol Coding	0.25	-0.55		

Table S2 (cont.): Summary of studies included in meta-analysis

Study	Sample	Currently taking antipsychotics	Sample Characteristics	Neuropsychological Assessment	Hedge's g	
					SA vs. SZ	SA vs. BD
<b>Lynham et al.</b> <sup>17</sup> <b>(cont.)</b>	188 SA (76 bipolar, 112 depressive)	77%	Stabilised outpatients DSM-IV	Animal Naming	0.15	-0.36
	558 SZ	86%		WMS III: Spatial Span	0.02	-0.34
	78 BD (68 type I & 10 type II / 59 with a history of psychosis & 19 without)	63%		Letter Number Span	0.19	-0.47
<b>Maj</b> <sup>18</sup>	16 SA (all depressive type) 20 SZ 20 HC		Inpatients and outpatients RDC	LNNB Motor	0.31	
				LNNB Rhythm	0.23	
				LNNB Tactile	0.13	
				LNNB Visual	0.31	
				LNNB Receptive Speech	0.32	
				LNNB Expressive Speech	0.43	
				LNNB Writing	0.35	
				LNNB Reading	0.41	
				LNNB Arithmetic	0.14	
				LNNB Memory	0.24	
				LNNB Intellectual Processes	0.18	
				LNNB Pathognomic	0.36	
				LNNB Left Hemisphere	0.27	
LNNB Right Hemisphere	0.23					
<b>Miller et al.</b> <sup>19</sup>	26 SA (9 bipolar, 17 depressive)	15/26 (58%)	Male veterans Inpatients	LNNB Motor	-0.35	
	26 SZ (8 paranoid, 3 undifferentiated, 4 residual, 1 disorganised)	15/26 (58%)	RDC	LNNB Rhythm	0.02	
				LNNB Tactile	0.05	
				LNNB Visual	-0.15	
				LNNB Receptive Speech	0.01	

Table S2 (cont.): Summary of studies included in meta-analysis

Study	Sample	Currently taking antipsychotics	Sample Characteristics	Neuropsychological Assessment	Hedge's g					
					SA vs. SZ	SA vs. BD				
<b>Miller et al.</b> <sup>19</sup> <b>(cont.)</b>	26 SA (9 bipolar, 17 depressive)	15/26 (58%)	Male veterans Inpatients	LNNB Expressive Speech	-0.44					
				LNNB Writing	-0.31					
	26 SZ (8 paranoid, 3 undifferentiated, 4 residual, 1 disorganised)	15/26 (58%)	RDC	LNNB Reading	-0.18					
				LNNB Arithmetic	-0.51					
				LNNB Memory	-0.36					
				LNNB Intellectual Processes	-0.08					
				LNNB Pathognomic	0.05					
				LNNB Left Hemisphere	0.03					
				LNNB Right Hemisphere	-0.08					
				BVRT	-0.53					
				RAVLT (trials 1-5)	-0.09					
	WAIS-R Verbal IQ	-0.24								
	WAIS-R Performance IQ	-0.21								
<b>Mueser et al.</b> <sup>20</sup>	52 SA 51 SZ 36 BD		Outpatients aged 50 or older DSM-IV	Administered the DKEFS battery and derived factor scores (domains) using principal components analysis:						
				Memory	0.09	-0.21				
				Verbal Fluency	0.22	-0.20				
				Psychomotor Speed	0.27	0.14				
				Executive Functioning	0.24	-0.23				
<b>Owoso et al.</b> <sup>21</sup>	63 SA 188 SZ 268 HC		Outpatients DSM-IV-TR	CNTRICS: Dot Probe Expectancy	-0.07					
				<b>Pinna et al.</b> <sup>22</sup>	66 SA 46 SZ	66/66 (100%) 43/46 (93%)	Outpatients DSM-IV-TR	MMSE	0.05	
								BACS Verbal Memory	0.21	
				BACS Working Memory	0.02					

Table S2 (cont.): Summary of studies included in meta-analysis

Study	Sample	Currently taking antipsychotics	Sample Characteristics	Neuropsychological Assessment	Hedge's g	
					SA vs. SZ	SA vs. BD
<b>Pinna et al.</b> <sup>22</sup>	66 SA	66/66 (100%)	Outpatients DSM-IV-TR	BACS Letter Fluency	0.28	
	46 SZ	43/46 (93%)		BACS Semantic Fluency	0.18	
				BACS Symbol Coding	-0.07	
				BACS Tower of London	0.03	
<b>Savage et al.</b> <sup>23</sup>	20 SA	100%	Outpatients DSM-IV	SDMT	0.45	
	41 SZ (20 paranoid, 21 undifferentiated)	100%		Anomalous Sentences Repetition Test	0.15	
				TMT A	0.67	
				TMT B	0.24	
				COWAT	0.51	
<b>Simonsen et al.</b> <sup>24</sup>	27 SA	25/27 (93%)	Inpatients and outpatients DSM-IV	WMS-III Logical Memory	0.26	-0.27
	102 SZ	93/102 (91%)		CVLT	0.12	-0.62
	136 BD (75 with history of psychosis & 61 without / 80 Type-I & 56 Type-II)	50/75 (67%) with psychosis & 12/61 (20%) without psychosis		WAIS-III Digit Symbol	0.07	-0.58
				WAIS-III Backward Digit Span	0.10	-0.27
				WM-MA 2-back	-0.04	-0.40
				D-KEFS Phonetic Fluency	0.10	-0.15
				D-KEFS Semantic Fluency	-0.13	-0.53
				D-KEFS Set Shifting	-0.08	-0.51
				D-KEFS Colour-Word Interference	-0.08	-0.60
<b>Stip et al.</b> <sup>25</sup>	13 SA		Outpatients DSM-IV	CANTAB Motor Screening	0.67	
	44 SZ			CANTAB Reaction Time	-0.02	
				CANTAB Stockings of Cambridge	-0.20	
				CANTAB Paired Associates Learning	0.40	

Table S2 (cont.): Summary of studies included in meta-analysis

Study	Sample	Currently taking antipsychotics	Sample Characteristics	Neuropsychological Assessment	Hedge's g	
					SA vs. SZ	SA vs. BD
<b>Studentkowski et al.</b> <sup>26</sup>	28 SA 32 BD		DSM-IV Outpatients	d2 Test (concentration)		-0.14
				TMT A		-0.63
				TMT B		-0.48
				WAIS Forward Digit Span		-0.59
				WAIS Backward Digit Span		-0.25
				WAIS Forward Block Span		0.72
				WAIS Backward Block Span		-0.64
				VLMT		-0.73
<b>Szoke et al.</b> <sup>27</sup>	25 SA 48 SZ 92 BD (52 with history of psychosis & 40 without) 48 HC		Inpatients (recruited prior to discharge) DSM-IV	WCST	0.27	-0.65
<b>Torniainen et al.</b> <sup>28</sup>	62 SA (52 bipolar, 10 depressive) 218 SZ 123 HC	54/62 (95%) 204/218 (95%)	Outpatients DSM-IV	WAIS-R: Vocabulary	0.44	
				WAIS-R: Digit Symbol	0.42	
				TMT A	0.34	
				TMT B	0.03	
				WMS-R: Forward Digit Span	0	
				WMS-R: Backward Digit Span	0.19	
				WMS-R: Forward Visual Span	0.22	
				WMS-R Backward Visual Span	0.32	
				CVLT	0.60	

Table S2 (cont.): Summary of studies included in meta-analysis

Study	Sample	Currently taking antipsychotics	Sample Characteristics	Neuropsychological Assessment	Hedge's g	
					SA vs. SZ	SA vs. BD
Torrent et al. <sup>29</sup>	34 SA (bipolar) 41 BD (16 Type – I, 25 Type – II, no psychosis) 35 HC	12/34 (35%) 7/41 (17%)	Outpatients DSM-IV	WCST		-0.11
				SCWT		0.11
				WAIS Forward Digit Span		-0.13
				WAIS Backward Digit Span		0.06
				TMT A		-0.31
				TMT B		-0.54
				COWAT (FAS)		-0.38
				Category Fluency: Animal Naming		-0.48
				CVLT		-0.84
				Van Rheenen et al. <sup>30</sup>	33 SA 49 SZ 35 BD (all Type-I; 26 with psychosis, 9 without)	31/33 (94%) 48/49 (98%) 16/35 (46%)
<i>Digit Symbol Coding</i>						
<i>TMT A</i>						
<i>DKEFS Colour-Word Interference (word reading and colour naming)</i>						
Immediate Memory	0.92	0.51				
<i>BVMT-R (trial 1)</i>						
<i>HVLT-R (trial 1)</i>						
Learning	0.24	-0.07				
<i>BVMT-R (trials 1-3)</i>						
<i>HVLT-R (trials 1-3)</i>						
Semantic Memory	0.59	-0.67				
<i>Category Fluency: Animal Naming</i>						
Attention / Vigilance	0.19	0.05				
<i>CPT-IP</i>						



Table S2 (cont.): Summary of studies included in meta-analysis

Study	Sample	Currently taking antipsychotics	Sample Characteristics	Neuropsychological Assessment	Hedge's g	
					SA vs. SZ	SA vs. BD
<b>Van Rheenen et al.</b> <sup>30</sup> (cont.)	33 SA	31/33 (94%)	Outpatients	Working Memory	0.01	-0.03
	49 SZ	48/49 (98%)	DSM-IV-TR	<i>Letter-Number Span</i> <i>WMS: Spatial Span (backwards)</i>		
	35 BD (all Type-I; 26 with psychosis, 9 without)	16/35 (46%)		Executive Function <i>NAB Mazes</i> <i>DKEFS Colour-Word Interference (interference / switching blocks)</i>	0.18	0.26
<b>Varma et al.</b> <sup>31</sup>	35 SA		Outpatients	WCST (perseverative errors)	0.10	
	48 SZ		DSM-IV	SCWT	-0.03	
	48 HC			VMPT	-0.28	

\*Study not included in meta-analysis, as summary data and effect sizes were not reported. Note: Two authors responded to our requests for data. Eighteen studies not shown here were excluded due to combined diagnostic groups, ineligible cognitive assessments or for other reasons. Of these, there were 10 studies that combined diagnostic categories (e.g. schizophrenia and schizoaffective disorder as one, or schizoaffective disorder combined with other psychosis). The majority of these studies had very small samples of participants with schizoaffective disorder (N<20) and so we did not think it would be productive to request disaggregated data from these studies.

*Abbreviations:* BD, Bipolar Disorder; SA, Schizoaffective Disorder; SZ, Schizophrenia; BACS, Brief Assessment of Cognition in Schizophrenia; BADS, Behavioural Assessment of the Dysexecutive Syndrome; BVMT-R, Brief Visuospatial Memory Test - Revised; BVRT, Benton Visual Retention Test; CANTAB, Cambridge Neuropsychological Test Automated Battery; CCST, California Card Sorting Test; CNTRICS, Cognitive Neuroscience Test Reliability and Clinical Applications for Schizophrenia; COWAT, Controlled Oral Word Association Test; CPT-IP, Continuous Performance Test – Identical Pairs; CVLT, California Verbal Learning Test; D-KEFS, Delis-Kaplan Executive Function System; HRB, Halstead-Reitan Neuropsychological Battery; HVLN-R, Hopkins Verbal Learning Test – Revised; HVOT, Hooper Visual Organisation Test, LNNB, Luria-Nebraska Neuropsychological Battery; NAB, Neuropsychological Assessment Battery; RAVLT, Rey Auditory Verbal Learning Test; RCF, Rey Complex Figure Test; SCWT, Stroop Colour-Word Test; SDMT, Symbol Digits Modalities Test; TMT, Trail Making Test; TPT, Tactual Performance Test; VCAT, Verbal Concept Attainment Test; VITI, Wechsler's Individual Test of Intelligence, Serbian translation of WAIS; VLMT, Verbal Learning & Retention Test; WAIS-III, Wechsler Adult Intelligence Scale - Third Edition; WAIS-R, Wechsler Adult Intelligence Scale – Revised Edition; WCST, Wisconsin Card Sorting Test; WM-MA, Working

Memory – Mental Arithmetic Test; WMS-III, Wechsler Memory Scale – Third Edition; WMS-R, Wechsler Memory Scale – Revised Edition; WRAT, Wide Range Achievement Test.

**Table S3 Results of meta-regression analyses**

	<b>Schizophrenia &amp; Schizoaffective Disorder</b>				<b>Bipolar Disorder &amp; Schizoaffective Disorder</b>			
	N	B	95% CIs	p	N	B	95% CIs	p
<b>Age</b>	21	-0.06	-0.42 – 0.29	0.72	10	0.03	-0.45 – 0.5	0.92
<b>Age of Onset</b>	10	0.21	-0.2 – 0.62	0.31				
<b>Duration of Illness</b>	12	0.17	-0.27 – 0.6	0.45	7	-0.06	-0.51 – 0.4	0.81
<b>Years in Education</b>	14	0.1	-0.07 – 0.27	0.27				
<b>Sex</b>	17	0.02	-0.07 – 0.11	0.63	10	0.02	-0.16 – 0.19	0.84
<b>Psychosis</b>	13	0.06	-0.21 – 0.33	0.65	5	-0.37	-1.2 – 0.46	0.38
<b>Depression</b>	7	0.04	-0.69 – 0.77	0.91	6	-0.41	-0.97 – 0.15	0.15
<b>Negative Symptoms</b>	13	-0.08	-0.32 – 0.16	0.5	5	-0.27	-0.81 – 0.27	0.33
<b>Mania</b>					7	-0.07	-0.45 – 0.31	0.72
<b>Current antipsychotics</b>	13	-0.06	-0.18 – 0.07	0.36	7	0.09	-0.06 – 0.24	0.25

**Table S4 Pooled effect sizes for comparisons of domains between schizoaffective disorder and schizophrenia**

<b>Domain</b>	<b>Studies (N)</b>	<b>Participants (N)</b>	<b>g</b>	<b>95% CI</b>	<b>P</b>	<b>Q-test P</b>	<b>Bias</b>
<b>Verbal learning</b>	15	SZ: 2431 SA: 983	0.24	0.12 to 0.37	<1 x 10 <sup>-4</sup>	0.009	-0.15
<b>Visuospatial learning</b>	6	SZ: 923 SA: 344	0.20	0.02 to 0.38	0.03	0.22	-1.10
<b>Executive function</b>	21	SZ: 2741 SA: 1370	0.10	-0.02 to 0.22	0.1	7 x 10 <sup>-4</sup>	0.75
<b>Speed of processing</b>	16	SZ: 2874 SA: 1344	0.18	0.09 to 0.27	1 x 10 <sup>-4</sup>	0.09	0.48
<b>Verbal fluency</b>	9	SZ: 1849 SA: 724	0.14	0.02 to 0.26	0.03	0.125	0.19
<b>Working memory</b>	13	SZ: 2316 SA: 899	0.09	0.003 to 0.17	0.04	0.41	-0.44

Positive effect sizes indicate better performance in the schizoaffective disorder group.

**Table S5 Pooled effect sizes for comparisons of domains between schizoaffective disorder and bipolar disorder**

<b>Domain</b>	<b>Studies (N)</b>	<b>Participants (N)</b>	<b>g</b>	<b>95% CI</b>	<b>P</b>	<b>Q-test P</b>	<b>Bias</b>
<b>Verbal learning</b>	8	BD: 869 SA: 646	-0.42	-0.60 to -0.24	<1 x 10 <sup>-4</sup>	0.03	-1.14
<b>Executive function</b>	10	BD: 996 SA: 701	-0.36	-0.48 to -0.23	<1 x 10 <sup>-4</sup>	0.24	0.03
<b>Speed of processing</b>	7	BD: 824 SA: 621	-0.35	-0.53 to -0.16	2 x 10 <sup>-4</sup>	0.04	-2.64
<b>Verbal fluency</b>	7	BD: 827 SA: 626	-0.32	-0.43 to -0.21	<1 x 10 <sup>-4</sup>	0.64	-1.64
<b>Working memory</b>	8	BD: 875 SA: 647	-0.30	-0.41 to -0.19	<1 x 10 <sup>-4</sup>	0.56	0.82

Positive effect sizes indicate better performance in the schizoaffective disorder group.

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