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

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Abstract

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

Introduction

Schizophrenia and bipolar disorder have traditionally been considered to be discrete categories in diagnostic classification. In contrast studies examining clinical features, genetic risk and neuroimaging data suggest there are overlaps between these disorders (Craddock & Owen, 2010; Ivleva et al., 2013; Keshavan et al., 2011; Ruderfer et al., 2018). The intermediate diagnosis, “schizoaffective disorder” was introduced due to the observation that some patients exhibit symptoms of schizophrenia and mood disturbance (Jäger, Haack, Becker, & Frasch, 2011). Schizoaffective disorder can be separated into two distinct subtypes: depressive and bipolar. However, the relationship between schizoaffective disorder, including the two subtypes, and schizophrenia or bipolar disorder remains unclear. Investigating the nature and degree of the cognitive impairments associated with schizoaffective disorder may further elucidate the relationship between these psychotic disorders.

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

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

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

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

Our aim was to conduct meta-analyses to examine cognitive performance across the bipolar-schizophrenia diagnostic spectrum. Studies that compared the subtypes of schizoaffective disorder to schizophrenia and bipolar disorder were also reviewed. Our hypothesis was that cognitive impairments in schizoaffective disorder would be intermediate between those observed in bipolar disorder and schizophrenia. We further hypothesised that the depressive subtype of schizoaffective disorder would be associated with more severe cognitive impairments similar to schizophrenia, whilst impairments in the bipolar subtype would be less severe than those of schizophrenia but more impaired than those of bipolar disorder.

Methods

Study selection

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

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

The inclusion criteria included all full text publications that:

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

Recorded variables were:

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

4. Cognitive test or battery results.

Authors were contacted for missing data.

Neuropsychological variables

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

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

Statistical analyses

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

1. Schizoaffective disorder and schizophrenia (N=22)
2. Schizoaffective disorder and bipolar disorder (N=10)
3. Schizoaffective disorder and bipolar disorder with psychosis (N=4)
4. Schizoaffective disorder and bipolar disorder without psychosis (N=3)
5. Schizoaffective disorder – depressive type and schizophrenia (N=4)
6. Schizoaffective disorder – depressive type and bipolar disorder (N=3)
7. Schizoaffective disorder – bipolar type and schizophrenia (N=3)
8. Schizoaffective disorder – bipolar type and bipolar disorder (N=4)
9. Schizoaffective disorder – bipolar type and schizoaffective disorder – depressive type (N=2)

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

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

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

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

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

Results

Retrieved studies

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

Schizophrenia and schizoaffective disorder

Composite cognition effect sizes were calculated for 22 studies comparing schizoaffective disorder (n=1166) and schizophrenia (n=2851). Participants with schizoaffective disorder performed better than participants with schizophrenia based on composite cognition scores ($g=0.17$, $p<0.0001$, see Figure 2). Effect size distributions were homogeneous ($T^2=0\ .002$; $Q=22.64$, $p=0.36$) and there was no evidence of publication bias (Egger: bias = -0.23). Meta-regression analyses were conducted to investigate the influence of nine variables: age, sex, years in education, age of onset, duration of illness, antipsychotic use, psychotic, depressive and

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

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

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

Bipolar disorder and schizoaffective disorder

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

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

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

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

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

Subtypes of schizoaffective disorder

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

Discussion

The aim of this meta-analysis was to compare cognitive outcomes of schizoaffective disorder with schizophrenia and bipolar disorder. This is the first meta-analysis to compare cognitive performance of participants with schizoaffective disorder and bipolar disorder. It is also the first review that has examined whether the subtypes of schizoaffective disorder differ in cognitive outcomes compared to schizophrenia and bipolar disorder. Cognitive performance of participants with schizoaffective disorder was intermediate between those with bipolar disorder and schizophrenia. Meta-analyses of the subtypes of schizoaffective disorder indicated that participants with the depressive subtype had cognitive impairments closer in severity to those seen in participants with schizophrenia, whereas those with the bipolar subtype were more impaired than participants with bipolar disorder and less impaired than those with schizophrenia (see Figure 4). Participants with the depressive subtype had worse 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**

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-

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

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

Schizoaffective disorder and schizophrenia

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

Cognition across the three disorders

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

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

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

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

Limitations

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

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

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

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

Conclusions

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

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Conflicts of interest

None

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Figure Legends

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

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

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
Amann et al. [1]	26 SA (bipolar) 45 SZ 51 BD 65 HC	26/26 (100%) 44/45 (98%) 46/51 (90%)	Acutely unwell inpatients DSM-IV SA also met RDC	WMS-III Verbal Memory WMS-III Working Memory WMS-III Visual Memory BADS Total	0.37 0.02 0.26 -0.12	0.16 0.05 -0.07 0.12
Beatty et al. [2]	11 SA 10 SZ (3 paranoid, 7 undifferentiated)		Outpatients DSM-III-R	CCST free sorting (perseverative sorts)	0.26	
Birindelli et al. [3]	40 SA 64 SZ		Outpatients DSM-IV-TR In remission	CVLT (trials 1-5) TMT A TMT B WCST (perseverative errors)	0.56 0.08 0.21 0.43	
Bornstein et al. [4]	18 SA 55 SZ (28 paranoid, 27 non-paranoid) 52 HC		Primarily outpatients DSM-III-R	WAIS-R Verbal IQ WAIS-R Performance IQ HRB Category Test (no of errors) WCST (perseverative errors) VCAT Verbal Fluency Verbal WMS-R Spatial WMS-R HRB TPT Time HRB TPT Memory HRB TPT Location HRB Speech Perception HRB Seashore Rhythm HRB TMT A HRB TMT B	0.29 0.11 0.11 0.66 0.90 -0.26 0.42 -0.01 0.24 -0.55 0.47 0.22 0.17 0.13 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
Bornstein et al. [4] (cont.)	18 SA 55 SZ (28 paranoid, 27 non-paranoid) 52 HC		Primarily outpatients DSM-III-R	HRB Finger Tap (right) HRB Finger Tap (left) HRB Grooved Peg (right) HRB Grooved Peg (left) HRB Finger Agnosia (right) HRB Finger Agnosia (left) HRB Graphesthesia (right) HRB Graphesthesia (left)	0.19 0.34 0.40 0.05 0.54 0.35 0.42 0.29	
Chen et al. [5]	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 Working Memory Motor Speed Verbal Fluency Attention & Processing Speed Executive Function	-0.11 -0.17 0.57 -0.09 0.03 -0.04	-0.31 -0.22 -0.33 -0.33 -0.52 -0.46
DeRosse et al. [6]	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 CVLT COWAT Verbal Fluency: Animal Naming TMT A TMT B	0.004 0.33 -0.02 0.08 0.10 0.04	-0.27 -0.23 -0.06 -0.28 -0.08 -0.38
Evans et al. [7]	24 SA (depressive and bipolar subtypes) 115 SZ	20/24 (69%) 103/115 (67%)	Outpatients, including veterans DSM-III-R	Verbal Ability *Aphasia Screening Test* *WAIS-R Vocabulary* *Boston Naming Test* *WAIS-R Similarities* *Thurstone Written Fluency* *COWAT (FAS)*	-0.02	

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. [7] (cont.)	24 SA (depressive and bipolar subtypes) 115 SZ	Outpatients, including veterans DSM-III-R	Psychomotor Speed *TMT A* *WAIS-R Object Assembly* *WAIS-R Digit Symbol* *WAIS-R Block Design* *TPT* *Digit Vigilance Test (time)*	-0.16	
			Abstraction / Cognitive Flexibility *Booklet Category Test* *TMT B* *WCST*	-0.34	
			Attention *WAIS-R Digit Span* *Digit Vigilance Test (errors)*	-0.18	
			Learning and Incidental Memory *CVLT (trials 1-5)* *Figure Memory Test (learning)* *Story Memory Test (learning)*	-0.38	
			Retention *CVLT (long delay recall)* *Figure Memory Test (delayed)* *Story Memory Test (delayed)*	-0.32	
			Motor *Finger Tapping Test* *Grooved Pegboard Test* *Hand dynamometer*	-0.07	

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
Fiszdon et al. [8]	73 SA 199 SZ		Outpatients DSM-IV	WCST (% conceptual level) WAIS-III Digit Symbol WAIS-III Digit Span WMS-R Logical Memory I HVLT-R WMS-R Figural Memory	0.05 0.21 0.16 0.34 0.14 0.31	
Gilvarry et al. [9]	296 SA 223 SZ		Outpatients RDC	TMT A TMT B	0.02 -0.17	
Glahn et al. [10]	15 SA (depressive) 15 SZ 26 BD (11 with history of psychosis, 15 without psychosis) 32 HC	100% 100% 91% with psychosis, 13% without psychosis	Outpatients DSM-IV Mixture of symptomatic and remitted patients	WAIS-III Forward Digit Span WAIS-III Backward Digit Span	0.20 -0.08	-0.27 -0.38
Goldstein et al. [11]	20 SA 63 SZ (29 undifferentiated, 20 paranoid, 14 residual)	100% 100%	Male veterans Stabilised inpatients DSM-III-R	HRB Category Test HRB TPT TMT B WCST (errors) WAIS-R Information WAIS-R Digit Span WAIS-R Vocabulary WAIS-R Arithmetic WAIS-R Comprehension WAIS-R Similarities WAIS-R Picture Completion WAIS-R Picture Arrangement WAIS-R Block Design	0.72 0.31 0.56 0.14 0.27 -0.11 0.85 0.77 1.05 0.17 0.55 0.21 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
Goldstein et al. [11] (cont.)	20 SA 63 SZ (29 undifferentiated, 20 paranoid, 14 residual)	100% 100%	Male veterans Stabilised inpatients DSM-III-R	WAIS-R Object Assembly WAIS-R Digit Symbol	0.23 0.35	
Gooding & Tallent [12]	23 SA (19 bipolar, 4 depressive) 34 SZ (15 paranoid, 12 residual, 6 undifferentiated, 1 disorganised) 30 HC	21/23 (91%) 34/34 (100%)	Outpatients RDC	WCST (perseverative errors)	-0.18	
Heinrichs et al. [13]	48 SA 103 SZ 72 HC		Outpatients DSM-IV	WAIS-III Vocabulary WAIS-III Matrix Reasoning WAIS-III Letter-Number WAIS-III Symbol Search CVLT (trials 1-5) COWAT WRAT-3 Reading	0.70 0.50 0.53 0.63 0.65 0.46 0.44	
Hill et al. [14]	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 BACS Tower of London BACS Symbol Coding BACS Verbal Fluency BACS Digit Sequencing	0.05 0.38 0.33 0.14 0.10	-0.37 -0.24 -0.17 -0.32 -0.37
Leposavic et al. [15]	30 SA 31 SZ (paranoid) 30 HC	100% 100%	Stabilised inpatients ICD-10	VITI Information VITI Digit Span VITI Vocabulary	-0.23 -0.31 -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
Leposavic et al. [15] (cont.)	30 SA 31 SZ (paranoid) 30 HC	100% 100%	Stabilised inpatients ICD-10	VITI Arithmetic VITI Comprehension VITI Similarities VITI Picture Completion VITI Picture Arrangement VITI Block Design VITI Object Assembly VITI Digit Symbol MMSE TMT A TMT B HVOT RCF (delayed recall) RAVLT (total words) WCST (perseverative errors)	-0.65 -0.38 -0.08 -0.19 -0.07 -0.90 -0.85 -0.44 -2.42 0.16 -0.22 0.42 -0.34 0.22 -0.77	
Lewandowski et al. [16]	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
Lynham et al. [17]	188 SA (76 bipolar, 112 depressive) 558 SZ 78 BD (68 type I & 10 type II / 59 with a history of psychosis & 19 without)	77% 86% 63%	Stabilised outpatients DSM-IV	HVLT-R NAB: Mazes BVMT-R CPT-IP TMT A BACS: Symbol Coding	0.27 -0.05 0.26 0.23 0.17 0.25	-0.59 -0.51 -0.49 -0.30 -0.50 -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
Lynham et al. [17] (cont.)	188 SA (76 bipolar, 112 depressive)	77%	Stabilised outpatients DSM-IV	Animal Naming	0.15	-0.36
				WMS III: Spatial Span	0.02	-0.34
	558 SZ	86%		Letter Number Span	0.19	-0.47
	78 BD (68 type I & 10 type II / 59 with a history of psychosis & 19 without)	63%				
Maj [18]	16 SA (all depressive type)		Inpatients and outpatients RDC	LNNB Motor	0.31	
				LNNB Rhythm	0.23	
	20 SZ			LNNB Tactile	0.13	
	20 HC			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	
Miller et al. [19]	26 SA (9 bipolar, 17 depressive)	15/26 (58%)	Male veterans Inpatients RDC	LNNB Motor	-0.35	
				LNNB Rhythm	0.02	
	26 SZ (8 paranoid, 3 undifferentiated, 4 residual, 1 disorganised)	15/26 (58%)		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
Miller et al. [19] (cont.)	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	
Mueser et al. [20]	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
Owoso et al. [21]	63 SA 188 SZ 268 HC		Outpatients DSM-IV-TR	CNTRICS: Dot Probe Expectancy	-0.07	
Pinna et al. [22]	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
Pinna et al. [22]	66 SA 46 SZ	66/66 (100%) 43/46 (93%)	Outpatients DSM-IV-TR	BACS Letter Fluency BACS Semantic Fluency BACS Symbol Coding BACS Tower of London	0.28 0.18 -0.07 0.03	
Savage et al. [23]	20 SA 41 SZ (20 paranoid, 21 undifferentiated)	100% 100%	Outpatients DSM-IV	SDMT Anomalous Sentences Repetition Test TMT A TMT B COWAT	0.45 0.15 0.67 0.24 0.51	
Simonsen et al. [24]	27 SA 102 SZ 136 BD (75 with history of psychosis & 61 without / 80 Type-I & 56 Type-II) 280 HC	25/27 (93%) 93/102 (91%) 50/75 (67%) with psychosis & 12/61 (20%) without psychosis	Inpatients and outpatients DSM-IV	WMS-III Logical Memory CVLT WAIS-III Digit Symbol WAIS-III Backward Digit Span WM-MA 2-back D-KEFS Phonetic Fluency D-KEFS Semantic Fluency D-KEFS Set Shifting D-KEFS Colour-Word Interference	0.26 0.12 0.07 0.10 -0.04 0.10 -0.13 -0.08 -0.08	-0.27 -0.62 -0.58 -0.27 -0.40 -0.15 -0.53 -0.51 -0.60
Stip et al. [25]	13 SA 44 SZ		Outpatients DSM-IV	CANTAB Motor Screening CANTAB Reaction Time CANTAB Stockings of Cambridge CANTAB Paired Associates Learning	0.67 -0.02 -0.20 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
Studentkowski et al. [26]	28 SA 32 BD		DSM-IV Outpatients	d2 Test (concentration) TMT A TMT B WAIS Forward Digit Span WAIS Backward Digit Span WAIS Forward Block Span WAIS Backward Block Span VLMT		-0.14 -0.63 -0.48 -0.59 -0.25 0.72 -0.64 -0.73
Szoke et al. [27]	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
Torniainen et al. [28]	62 SA (52 bipolar, 10 depressive) 218 SZ 123 HC	54/62 (95%) 204/218 (95%)	Outpatients DSM-IV	WAIS-R: Vocabulary WAIS-R: Digit Symbol TMT A TMT B WMS-R: Forward Digit Span WMS-R: Backward Digit Span WMS-R: Forward Visual Span WMS-R Backward Visual Span CVLT	0.44 0.42 0.34 0.03 0 0.19 0.22 0.32 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. [29]	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 SCWT WAIS Forward Digit Span WAIS Backward Digit Span TMT A TMT B COWAT (FAS) Category Fluency: Animal Naming CVLT		-0.11 0.11 -0.13 0.06 -0.31 -0.54 -0.38 -0.48 -0.84
Van Rheenen et al. [30]	33 SA 49 SZ 35 BD (all Type-I; 26 with psychosis, 9 without)	31/33 (94%) 48/49 (98%) 16/35 (46%)	Outpatients DSM-IV-TR	Processing Speed *Digit Symbol Coding* *TMT A* *DKEFS Colour-Word Interference (word reading and colour naming)* Immediate Memory *BVMT-R (trial 1)* *HVLT-R (trial 1)* Learning *BVMT-R (trials 1-3)* *HVLT-R (trials 1-3)* Semantic Memory *Category Fluency: Animal Naming* Attention / Vigilance *CPT-IP*	0.24 0.92 0.24 0.59 0.19	-0.20 0.51 -0.07 -0.67 0.05

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
Van Rheenen et al. [30] (cont.)	33 SA 49 SZ 35 BD (all Type-I; 26 with psychosis, 9 without)	31/33 (94%) 48/49 (98%) 16/35 (46%)	Outpatients DSM-IV-TR	Working Memory *Letter-Number Span* *WMS: Spatial Span (backwards)*	0.01	-0.03
				Executive Function *NAB Mazes* *DKEFS Colour-Word Interference (interference / switching blocks)*	0.18	0.26
Varma et al. [31]	35 SA 48 SZ 48 HC		Outpatients DSM-IV	WCST (perseverative errors) SCWT VMPT	0.10 -0.03 -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; HVLT-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

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

Domain	Studies (N)	Participants (N)	g	95% CI	P	Q-test P	Bias
Verbal learning	15	SZ: 2431 SA: 983	0.24	0.12 to 0.37	$<1 \times 10^{-4}$	0.009	-0.15
Visuospatial learning	6	SZ: 923 SA: 344	0.20	0.02 to 0.38	0.03	0.22	-1.10
Executive function	21	SZ: 2741 SA: 1370	0.10	-0.02 to 0.22	0.1	7×10^{-4}	0.75
Speed of processing	16	SZ: 2874 SA: 1344	0.18	0.09 to 0.27	1×10^{-4}	0.09	0.48
Verbal fluency	9	SZ: 1849 SA: 724	0.14	0.02 to 0.26	0.03	0.125	0.19
Working memory	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

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

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

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