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Review

Cognitive trajectories following onset of psychosis: a meta-analysis

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Background

Cognitive impairment is a core feature of schizophrenia, associated with poor functional outcomes. The course of cognitive function in the years following illness onset has remained a subject of debate, with a previous analysis finding no worsening, providing support for the neurodevelopmental model of schizophrenia. Since then, many more studies have reported on longitudinal cognitive performance in early psychosis, with some indicating deterioration, which does not align with this view.

Aims

This study aims to quantitatively review the literature on the longitudinal trajectory of cognitive deficits in the years following psychosis onset, in comparison with healthy controls. It is the first to also synthesise longitudinal data on social cognition.

Method

Electronic databases ('PubMed', 'PsycInfo' and 'Scopus') were searched (to end September 2021). Meta-analyses of 25 longitudinal studies of cognition in early psychosis were conducted (1480 patients, 789 health controls). Unlike previous analyses, randomised controlled trials and those with multiple cognitive testing periods within the first year were excluded to minimise bias (PROSPERO, ID: CRD42021241525).

Results

Small improvements were observed for global cognition ($g = 0.25$, 95% CI 0.17–0.33) and individual cognitive domains, but these were comparable with healthy controls and likely an artefact of practice effects.

Conclusions

There is no evidence of continued cognitive decline or improvement in the early years following psychosis onset, with a need for more studies over longer follow-up periods. Practice effects highlight the importance of including control samples in longitudinal and intervention studies. Further data are needed to evaluate the course of social cognition subdomains.

Keywords

Early psychosis; schizophrenia; cognition; social cognition; cognitive remediation.

Background

Cognitive impairment is considered a core feature of schizophrenia,[1] and is associated with poor functional outcomes in multiple domains.[2,3] Meta-analyses and prospective cohort studies have detected a medium-sized (8–9 IQ point) impairment in premorbid IQ in those who go on to develop schizophrenia,[4,5] and an even larger impairment (14–15 IQ points) following symptom onset.[4,6] Although impairment affects almost all cognitive domains,[7] there is evidence of slight variations in the degree of impairment, with replicated findings that memory, executive functions, attention and processing speed domains are the most compromised.[6,8,9] As a result of an historical lack of longitudinal cohort studies, the course of cognitive impairment has been largely estimated by cross-sectional studies of groups at different illness development stages.[5,6,10–12]

The trajectory of cognitive impairments following a first episode of psychosis has been the centre of debate about whether cognitive impairment is insidious, developing gradually over time, or whether cognitive dysfunction begins early, with critical periods of rapid decline prior to, and in the early years following, onset of symptoms with stability thereafter.[13] The early years following a first episode of psychosis have been proposed as a 'critical period' for recovery in which individuals can make the greatest improvement in social functioning.[14–16] Understanding the course of cognitive functioning therefore has important implications for consideration of difficulties at different illness stages, and for the development and optimisation of intervention strategies.

A previous meta-analysis examined the progression of cognitive deficits within the first 5 years following first episode of psychosis onset, including longitudinal studies up until February 2013.[17] The lack of evidence of continued cognitive decline provided support for a neurodevelopmental risk-factor model of schizophrenia,[18,19] rather than a neurodegenerative model characterised by a chronic active illness progression.[20,21] However, potentially because of the scarcity of studies, this meta-analysis included randomised controlled studies and those in which cohorts had undergone several cognitive testing visits within the first year, increasing the likelihood of treatment and practice effects playing a role.

Aims of the current study

Almost a decade on, many more cohort studies have reported on cognitive performance in the years following a first episode of psychosis. Some provided data that do not align with the neurodevelopmental risk-factor model as they indicate worsening performance in some domains,[22–24] whereas others indicate cognitive stability or improvement across all domains.[25,26] The focus of this meta-analysis is to comprehensively review the literature on the longitudinal trajectory of cognitive deficits in the early years following psychosis onset. This study will only consider longitudinal cohort studies to exclude potential forms of bias such as randomisation to trial arms. Multiple exposure bias will be controlled by including only the results from the most recent assessment after baseline, with a minimum of 12 months between assessments to minimise practice effects. In addition to cognitive domains previously covered in meta-analyses this study will be the first, to our knowledge, to synthesise longitudinal data on social cognition that has been shown to have a stronger relationship with social functioning than cognition.[27,28] As in Bora & Murray (2014),[17] this meta-analysis will include longitudinal studies examining cognitive changes within the proposed 'critical period' 1–5 years following psychosis onset,

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when confounding effects of longer-term illness (such as medication) are likely to be minimised.[14] Potential moderators of cognitive change will also be explored.

The findings of this meta-analysis will provide evidence on the evolution of global, domain and task-specific cognitive impairments over time. Relative stability is thought to provide support for the neurodevelopmental theory of schizophrenia, whereas continued cognitive decline is considered to fit with a neurodegenerative model. The findings have implications for the implementation and optimisation of interventions targeting cognitive difficulties such as cognitive remediation therapy, which have been shown to effectively target cognitive processes and improve social functioning.[29,30]

Method

Protocol and registration

This review follows the PRISMA guidelines for reporting systematic reviews.[31] The protocol was pre-registered on the PROSPERO registry, ID: CRD42021241525 on 22 March 2021.

Search strategy

The following three electronic databases were searched up to the end of September 2021: 'PubMed', 'PsycINFO', and 'Scopus', using the following search terms: to identify participants: ('psychosis' OR 'schizophrenia' OR 'schizo*' OR 'FEP' OR ('first episode psychosis') AND to identify cognitive measures: ('cog*', 'neurops*' OR 'neurocognit*' OR 'memory' OR 'attention', OR 'executive' or 'processing OR 'social cog', OR 'social knowledge' OR 'attribution bias' OR theory of mind' OR 'social perception') AND to identify the study design: ('longitudinal' OR 'follow-up' OR 'chang*' OR 'course' OR 'trajectory'). Article titles and abstracts were reviewed to identify relevance, with full texts then being examined. A backwards reference search of included articles was performed manually to identify additional studies meeting the inclusion criteria.

Inclusion/exclusion criteria

Inclusion criteria were studies that:

(a) are published in an English language peer-reviewed journal;
(b) report longitudinal cognition data;
(c) used at least one standardised test at two time points;
(d) had a minimum follow-up period of 12-months; and
(e) included participants with a first episode of psychosis, defined as being within 5 years of their first psychosis episode at the time of the initial assessment.

Inclusion criteria for follow-up duration was 1–5 years from initial assessment.

Exclusion criteria were:

(a) multiple reports of the same data (in which case the study reporting the earliest cognitive assessment follow-up was included);
(b) unpublished studies, reviews, conference abstracts or case reports;
(c) studies not reporting quantitative data;
(d) studies using a non-standardised test;
(e) controlled intervention studies (i.e. randomised control intervention studies);
(f) studies conducting additional cognitive follow-up testing before the minimum follow-up period (e.g. at 6 months); these were excluded to minimise practice effects; or
(g) studies conducted in early-onset psychosis (age < 16 years).

Screening

After removing duplicates two authors (A.J.W., L.H.) independently screened all titles and abstracts for eligibility. Full texts for eligible papers were also further screened for eligibility by the same authors and disagreements resolved by a third author.

Data extraction

Study sample size, follow-up duration, mean age, gender (% male), sample diagnoses, % on antipsychotic medication, cognitive tasks used, cognitive data (baseline and follow-up) and positive and negative symptom scores (baseline and follow-up) were extracted independently by two authors, for inclusion in main and moderator analyses. For comparison with the psychosis group, the same variables were also extracted for healthy controls. A comprehensive analysis of test–retest scores in healthy controls was beyond the scope of this study, so healthy control data were restricted to data from the papers included in the main analysis

Cognitive measures

Where studies reported cognitive domain summary scores (e.g. processing speed), these were extracted directly from articles. Where only individual tests scores were reported, these were assigned to predefined cognitive domains. As there is little consensus on how individual tests map onto cognitive domains, assignment was guided by the articles and broader literature. For studies with multiple tests measuring the same neuropsychological construct (e.g. WAIS-Digit Symbol Substitution Test and Trail Making Task A), a single domain summary measure (i.e. processing speed) was calculated by averaging effect sizes. We also computed a global cognition score using source data where possible, and where no summary measure was reported, effect sizes of all neuropsychological measures were pooled (where at least two seperate domains were measured). For a full list of domains and allocation of specific cognitive tasks, see Supplementary S1 and Supplementary Table S1, available at https://doi.org/10.1192/bjp.2022.131.

Study quality

The Newcastle–Ottawa Scale[32] was used to assess the quality of each included study. This is a commonly used tool for non-randomised studies and includes a quality rating for: selection, comparability and exposure/outcome. Studies are given a star rating from zero to nine. Data quality was rated by authors A.J.W. and L.H.

Meta-analytic procedure

Meta-analyses were conducted using the 'Metafor' statistical package for R.[33] Using data reported in each study, standardised mean differences were estimated by subtracting average scores at follow-up from average scores at baseline, and dividing the result by the pooled standard deviation, with a small sample correction taking each sample size into consideration (Hedges' unbiased *g*).[34] This approach is used to avoid the overestimation of the magnitude of effect in meta-analyses of longitudinal studies.[35] Where more than three studies reported data for the same cognitive task, individual measure meta-analyses were performed. This has the advantage of identifying changes in specific cognitive processes (e.g. immediate versus delayed recall) and limits heterogeneity. Where samples overlap, the study with the largest overall sample size was included. In addition, to establish the presence of cognitive impairment at baseline, patient and healthy control groups were compared on baseline cognitive function for each domain using the same analytic procedure, but with the inclusion of baseline cognitive scores for each group.

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Distributions of effect sizes were expected to be heterogeneous in cognitive studies in this population, so a random-effects model (DerSimonian–Laird estimate) was used, with effect sizes weighted using the inverse variance method. Heterogeneity of effect size distributions was measured using the *Q*-test, and the extent of heterogeneity reported using the I^2 statistic.[36] I^2 quantifies the percentage of total variation across studies considered to be because of heterogeneity rather than chance. I^2 values indicate low (25%), moderate (50%), and (75%) high heterogeneity.[36] In analyses with at a minimum of ten studies, publication bias was assessed using inspection of forest plots and Egger's test. All results in the analyses are presented so that positive values reflect improved performance at follow-up.

Subgroup sensitivity analyses

The Q_{bet}-test was used to compare patient versus healthy control change in cognition, and additionally to compare non-affective only versus mixed-affective studies. This method maximises the number of included studies, although it can inflate the variance of the estimates. As such, a sensitivity analysis was also performed calculating patient–control effect size for change (standardised mean difference in change scores from baseline to follow-up) for only studies including both patient and control groups. Results were screened for outliers using the find.outlier function in the {dmetar} package that implements an outlier detection and removal algorithm of studies with confidence intervals that do not overlap with the confidence interval of the pooled effect. Outlier influence on results was investigated using leave-one-out analysis (effect size and I^2). Domain and task outliers are listed in Supplementary Table S2.

Meta-regressions

To identify the influence of potential moderators, meta-regression analyses were conducted for cognitive domains, using a restricted-maximum-likelihood random-effects model. Potential moderators of change were, mean age, percentage of male participants, mean years of education, percentage of participants on antipsychotic medication, study follow-up duration (months), change in positive and negative symptom severity scores (% after adjusting for non-zero floor), and baseline positive and negative symptoms scores. Where there were not enough studies with data to meet the minimum threshold for analysis ($n < 10$)[36] meta-regression analyses were not performed. Studies including only age-adjusted scores, were not included when considering age as a moderator.

Results

Search outcome

After removing duplicates, intervention studies, papers that only measured cognition once, did not use standardised tests or did not fulfil other criteria, 25 full-text papers from the 1780 abstracts were left for the meta-analyses (see Fig. 1 and Supplementary Table S3). Owing in part to the inclusion criteria (e.g. use of standardised tests), all studies scored similarly on the Newcastle–Ottawa scale and were of good quality. Sensitivity analyses by study quality were therefore not performed.

Sample demographics

Included studies had 1480 participants with early psychosis, a mean age 24.85 years, 62.84% of participants were men and they had a mean of 20.76 months between baseline and follow-up assessments. For comparison, 13 studies included data for healthy controls, with 789 participants, a mean age of 25.45 years, an average of 60.82% men, and with 19.60 months between baseline and follow-up assessments. Where data were available, patients showed a mean reduction of 48.9% in positive symptoms and 18.7% in negative symptoms between baseline testing and follow-up. Study characteristics are detailed in Supplementary Table S3.

Patient–control differences at baseline

Large cognitive impairments were present in the patient group compared with healthy controls at baseline, including for global cognition ($g = 0.85$) (Table 1). See Supplementary S4 for further description.

Change in cognition

Patient samples showed significant improvement in 7 out of the 11 domains (Table 2), including global cognition (Fig. 2) (see Supplementary S5 for further description). In comparison with healthy controls, effect sizes of change were identical for global cognition (0.25) and the Q_{bet}-test was non-significant for all domains (Table 2). The Q_{bet} tests for verbal learning and memory remained non-significant even after separate analysis with the exclusion of clear outliers ($Q_{bet} = 0.23$, $P = 0.63$). Average follow-up period was similar for patients and controls (Supplementary Table S4). Results did not differ in the sensitivity analyses comparing standardised mean difference in change scores from baseline to follow-up, in only studies including both patient and control groups (Supplementary Table S5).

Moderators

There were no significant moderators, except for working memory, where a higher percentage of men was associated with less improvement between time points ($z = 2.14$, $P = 0.03$). In the sensitivity analysis comparing non-affective versus mixed samples, there was significantly less improvement in attention and vigilance in the mixed-affective studies ($Q = 5.14$, $P = 0.02$). All other comparisons were non-significant (Supplementary Tables S7 and S8).

Task-specific analyses

Q_{bet}-test comparisons with healthy control samples were non-significant for all tasks and remained non-significant even after the exclusion of clear outliers. Further description of change in patients and healthy controls can be found in Supplementary S9.

Discussion

Main findings

This meta-analysis is the first, to our knowledge, to comprehensively examine cognitive change in the early years following the onset of psychosis across all cognitive domains in studies of good quality and little risk of bias from treatment and practice effects.

The patient groups were impaired on all cognitive domains at baseline, with large effect sizes for global cognition and large or medium effect sizes for all other domains. Over time, only modest improvements were seen in global cognitive performance, with an effect size identical to that in healthy controls, indicating that any improvement may be an artefact of practice. Small improvements were also seen across specific domains and tasks, including social cognition, but improvement did not significantly differ from that in healthy controls despite healthy controls already performing significantly better across all tasks. There were insufficient data to examine subdomains of social cognition (theory of mind, attribution bias, social perception, emotion perception/recognition) with

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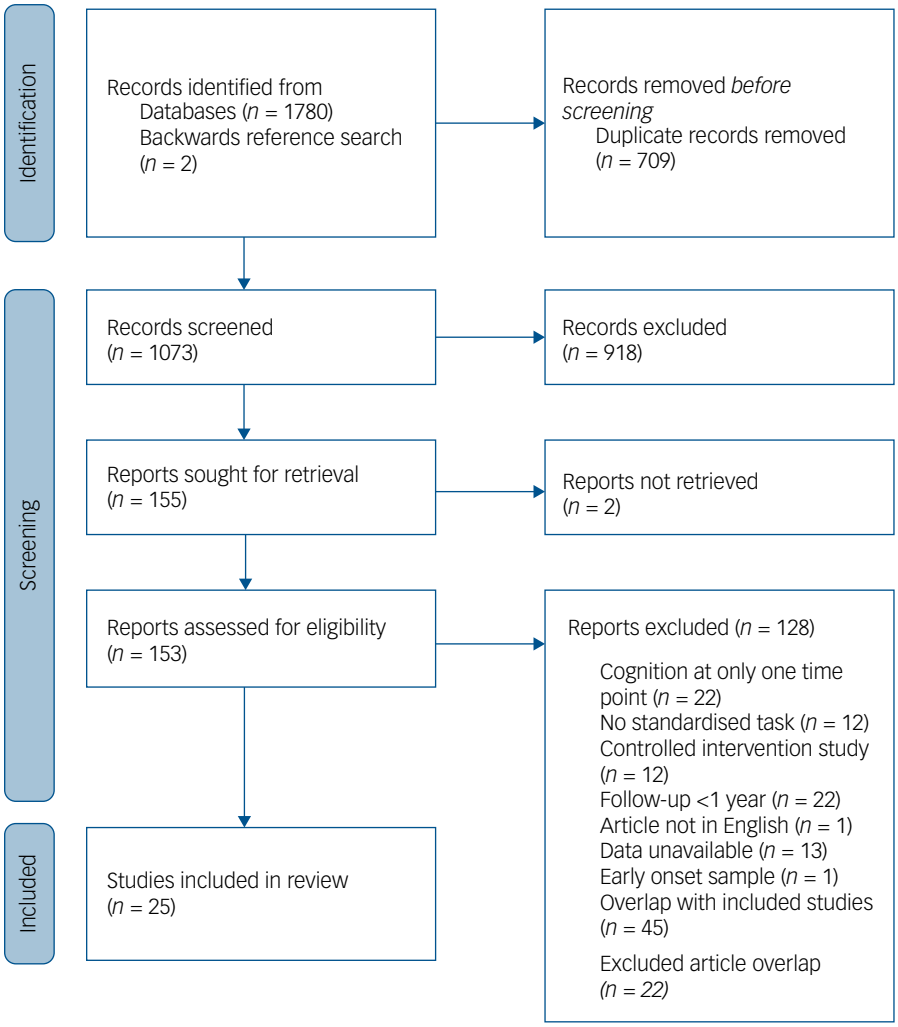

Fig. 1 PRISMA flow diagram.

further research needed to discern whether there is stability or change. Lack of significant improvements were in the same domains in both the healthy controls and patient groups (construction and visuospatial skills, and visual learning and memory), and those where patients are thought to be less impaired (motor skills). The exception was verbal fluency, where, in contrast to controls, patients showed no significant improvement. Improvement in symptoms did not moderate change in global cognition, in keeping with findings of other studies.[40,51] Somewhat surprisingly, sensitivity analysis showed significantly less improvement in attention and vigilance in mixed (affective and non-affective) studies, compared with non-affective-only samples. Results were not undermined by publication bias or high heterogeneity.

Comparison with the existing literature

Overall, these findings support the neurodevelopmental risk-factor hypothesis and earlier longitudinal and cross-sectional meta-analyses.[6,17] Much of the cognitive impairment seen in psychosis occurs prior to the onset of illness and remains relatively stable following symptom onset. Despite the exclusion of controlled trials, effect sizes for domain improvements were comparable with those

Table 1 Meta-analyses of baseline patient versus control differences in cognitive domains[a]

Domain	*k*	*n*	Estimated effect (g)[b]	95% CI	*Z*	*P*	*Q*	*Q* (*P*)	R^2	I^2%	Bias (*P*)
Global cognition	11	1536	0.85	0.63–1.07	7.52	<0.001	28.45	0.001	0.08	64.8	0.74
Speed of processing	10	1348	1.24	0.92–1.56	7.60	<0.001	54.46	<0.001	0.21	83.5	0.16
Reasoning and problem solving	10	1479	0.83	0.67–0.98	10.53	<0.001	13.09	0.101	0.02	38.9	0.77
Attention and vigilance	8	1140	0.66	0.43–0.88	5.67	<0.001	16.74	0.010	0.06	64.2	–
Working memory	7	868	0.83	0.63–1.03	8.31	<0.001	15.58	0.016	0.04	61.5	–
Verbal learning and memory	9	1289	1.14	0.89–1.39	9.03	<0.001	28.35	<0.001	0.10	71.8	–
Visual learning and memory	5	696	0.80	0.50–1.10	5.23	<0.001	11.25	0.024	0.07	64.4	–
Social cognition	4	512	0.59	0.35–0.84	4.7	<0.001	4.83	0.185	0.02	37.8	–
Verbal fluency	7	1281	0.97	0.78–1.16	10.19	<0.001	12.4	0.056	0.03	51.6	–

a. All effect sizes indicate better performance in healthy controls. b. Estimated effect (*g*) difference in performance between patients and healthy controls at baseline. *Q* is the measure of the heterogeneity of the distribution of effect size. I^2 quantifies the percentage of total variation across studies because of heterogeneity. Bias is the *P*-value of Egger's test.

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Table 2 Meta-analyses of change in cognition across domains, for patient and healthy controls of included samples[a]

Domain	*k*	*n*	Estimated effect (*g*)	95% CI	*Z*	*P*	*Q*	*Q* (*p*)	R^2	I^2%	Bias (*P*)	Q_{bet} (*P*)
Global cognition												
Patients	19	1326	0.25	0.17 to 0.33	5.97	<0.001	7.98	0.98	0	0	0.27	0.00 (0.98)
Health controls	11	740	0.25	0.14 to 0.35	4.60	<0.001	4.96	0.89	0	0	0.07	
Speed of processing												
Patients	13	958	0.20	0.10 to 0.29	4.12	<0.001	9.80	0.63	0	0	0.72	2.42 (0.30)
Health controls	10	633	0.31	0.19 to 0.44	3.95	<0.001	10.00	0.35	9	10	0.93	
Reasoning and problem solving												
Patients	17	1245	0.30	0.20 to 0.41	5.53	<0.001	22.48	0.13	0.01	29	0.05	2.84 (0.24)
Health controls	10	711	0.18	0.07 to 0.29	3.27	0.001	4.00	0.91	0	0	0.55	
Attention and vigilance												
Patients	10	863	0.31	0.21 to 0.40	6.32	<0.001	7.73	0.56	0	0	0.37	0.21 (0.65)
Health controls	7	557	0.27	0.10 to 0.43	3.12	0.002	9.50	0.14	0.02	37	–	
Working memory												
Patients	12	844	0.15	0.02 to 0.28	2.32	0.02	16.51	0.24	0.02	32	0.84	0.02 (0.88)
Health controls	9	537	0.16	0.05 to 0.28	2.71	0.01	5.41	0.71	0	0	–	
Verbal learning and memory												
Patients	12	953	0.24	0.10 to 0.37	3.46	0.001	20.43	0.04	0.02	46	0.56	0.02 (0.89)
Health controls	7	508	0.20	–0.01 to 0.42	1.92	0.06	13.57	0.03	0.04	55	–	
Visual learning and memory												
Patients	8	360	0.10	–0.05 to 0.25	1.29	0.19	2.94	0.82	0	0	–	1.40 (0.24)
Health controls	5	340	0.21	–0.01 to 0.43	1.91	0.06	6.62	0.16	0	40	–	
Social cognition												
Patients	7	413	0.25	0.11 to 0.39	3.43	0.001	5.51	0.48	0	0	–	0.03 (0.86)
Health controls	4	293	0.20	0.00 to 0.40	1.92	0.06	3.72	0.29	0	19	–	
Verbal fluency												
Patients	12	997	0.11	–0.01 to 0.23	1.76	0.08	16.45	0.13	0.01	33.1	0.65	0.88 (0.35)
Health controls	7	574	0.19	0.07 to 0.30	3.12	0.002	1.62	0.95	0	0	–	
Verbal and language skills												
Patients	3	103	0.29	0.00 to 0.58	1.98	0.05	0.16	0.93	0	0	–	–[b]
Health controls	–	–	–	–	–	–	–	–	–	–	–	
Construction and visuospatial skills												
Patients	3	328	0.02	–0.13 to 0.18	0.31	0.76	1.47	0.48	0	0	–	–[b]
Health controls	3	232	0.22	–0.18 to 0.62	1.09	0.28	7.61	0.02	0.09	74	–	
Motor skills												
Patients	3	393	0.07	–0.07 to 0.21	0.94	0.35	0.10	0.95	0	0	–	–[b]
Health controls	–	–	–	–	–	–	–	–	–	–	–	

a. Estimated effect (*g*) improvement in performance from first assessment to follow-up. *Q* is measure of the heterogeneity of the distribution of effect size. I^2 quantifies the percentage of total variation across studies due to heterogeneity. Bias is the *P*-value of Egger's test. Qbet is the comparison of change in patients versus healthy controls. Results reported before any exclusion of outliers. Forest plots for each domain are available in Supplementary S6.
b. Not enough data.

of Bora & Murray (2014)[17] (0.02–0.31 in this analysis versus 0.13–0.38 in Bora & Murray[17]). Both studies showed least improvement compared with controls in processing speed, working memory and verbal fluency. Greatest improvement was seen in executive function, using the Wisconsin Card Sorting Test, potentially indicating greatest malleability in problem-solving skills.

Given that large-scale meta-analyses have shown cognitive deficits in childhood or adolescence prior to detectable symptoms[5,7,53] with greater deviation from controls at the time of first episode,[6] there remains the question of when cognitive decline occurs. One explanation accounting for the discrepancy between pre- and post-onset cognitive deficits, is the model of progressive neurodevelopmental impairment[54] suggesting increasing cognitive 'lag' seen following critical developmental periods.[55] Others argue that cognitive worsening takes place during a prodromal period, with some studies showing evidence of cognitive worsening at this stage,[13] while other studies found no evidence.[56,57] Harvey[58] argues that inconsistencies may be related to the conceptualisation of when a first episode begins, with sensitive prodromal measures potentially capturing the first stages of psychotic illness, previously considered to be prodromal.

Although our meta-analysis shows no cognitive improvement above that of healthy controls, debate remains around the trajectory of cognitive impairment over longer periods. A study by Zanelli et al,[59] assessing individuals with a first episode of psychosis at 10-year follow-up, found that compared with healthy participants, patients with schizophrenia showed a significant decline in IQ and in tasks assessing memory and verbal knowledge, even after controlling for gender, age, ethnicity and education. Similarly, an 18-year follow-up study, Fett et al,[60] found continued cognitive decline across multiple, but not all domains, and there is evidence of a slightly larger (15–21 IQ point) deficit in those with long-standing schizophrenia.[10,12,61] These findings raise the question of whether cognitive impairment in schizophrenia results from both abnormal development and later deterioration only detectable over long-periods, with later deterioration differing between cognitive functions. One possible explanation for this is that psychosis may lead to longer periods of restricted activity and opportunities to use cognitive skills, leading to a decline over time. Against this, other studies assessing individuals with psychosis over 10 years found no worsening of deficits after illness onset[62–64] with some evidence that any progression may be because of medication[29,65,66] or lifestyle factors.[67,68]

Further complexity in assessing cognition over time comes from individual heterogeneity,[69] which may be obscured when assessing group means,[26] as well as the potential for those who make good recoveries being underrepresented in studies with longer follow-up periods.[70] Our analysis shows that study quality has remained high, although this is limited by the exclusion of many studies because of multiple testing within the first year ($n = 22$). Of the studies including non-affective samples, four (out of six) were conducted since the Bora and Murray (2014)[17] analysis, highlighting

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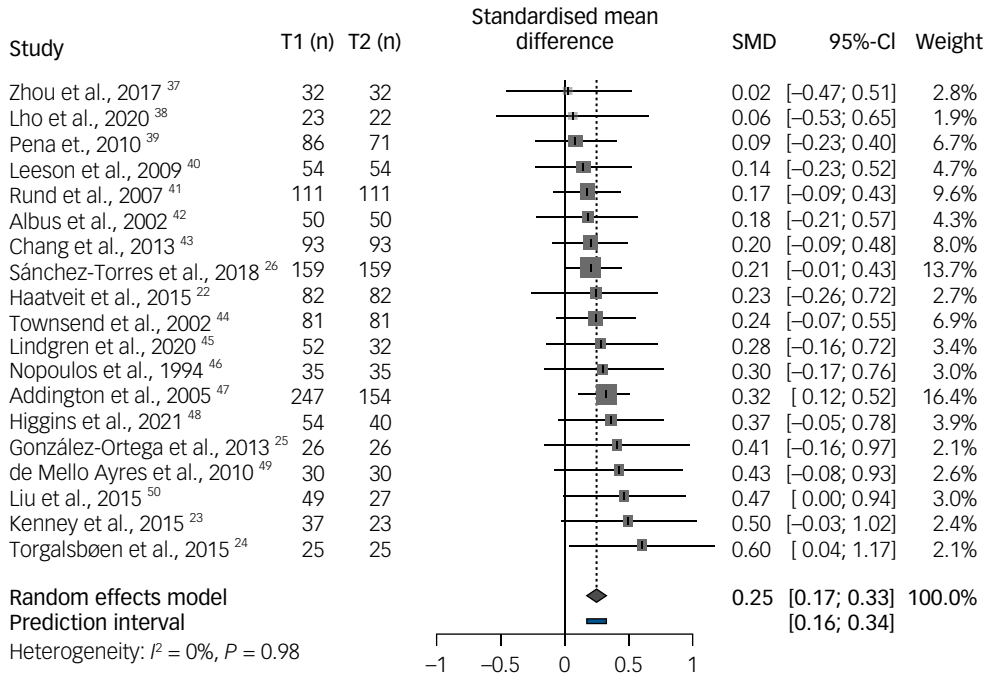

Fig. 2 Forest plot showing change in global cognition in the patient samples (standardised mean difference (SMD) is Hedges' *g*); *P*-value is for *Q*-test; diamond, overall estimate. T_1, baseline; T_2, follow-up.

some studies still include mixed diagnoses in their inclusion criteria, although the proportion of patients with affective diagnoses was low. There remains a need for studies to assess cognition in affective-first-episode psychosis independently. Resolving these issues is important, with implications for the course of illness, as well as consideration of those most suited to benefit from interventional strategies aimed at preserving and improving cognition in people with psychosis.[29,30,71] Finally, evidence for comparable improvement in cognitive test performance in healthy controls has implications for assessing cognitive change both clinically and in randomised controlled trials, highlighting the importance of using control groups when drawing conclusions about intervention efficacy.

Limitations

Limited healthy control data meant comparison with patient groups was not possible for all domains or tasks. Similarly, meta-regressions and sensitivity analyses could not be performed for all domains because of inadequate data, including for antipsychotic dose, which may moderate cognitive change. Social cognition tests varied across studies, many of which have since been shown to have poor psychometric properties.[72] Grouping social cognition constructs prohibits conclusions being made about these subdomains, particularly given the potential for their separate factor structures[73] and neural bases.[74] Categorisation of cognitive tasks also remains a wider issue, with no consensus across studies as to the cognitive domains that tasks are most accurately measuring. It should also not be discounted that ceiling effects may have minimised improvement in healthy control performance, and that this might mask areas of relative deterioration in the patient group. Finally, subgroup analyses have been shown to lack statistical power to detect group differences, which might be observed with more available studies,[75] however, comparison of confidence intervals and careful interpretation do not change the conclusions of this analysis.

Implications

We found no evidence of cognitive decline in the early years following psychosis onset. Small improvements were observed across individual cognitive domains and tasks, but these were in line with those seen in healthy comparison groups and are likely an artefact of practice effects. Further data are needed to evaluate the course of social cognition subdomains following onset of psychosis. We conclude that there is no evidence of continued cognitive decline or improvement in the early years following psychosis onset, with a need for more studies over longer follow-up periods. Evidence of practice effects highlights the importance of including control samples in longitudinal and intervention studies measuring cognition at multiple time points.

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Supplementary material

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Data availability

The data that support the findings of this study are available from the corresponding author, A.J.W., upon reasonable request.

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Author contributions

Conception and design of the work was by A.J.W., M.C., T.W. and A.P. Data search and extraction were performed by A.J.W. and L.H. Analyses were conducted by A.J.W., with supervision by M.C. and A.P. All authors made significant contributions to drafting and/or revising the manuscript.

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Declaration of interest

None.

References

1 Green MF, Horan WP, Lee J. Nonsocial and social cognition in schizophrenia: current evidence and future directions. *World Psychiatry* 2019; **18**: 146–61.

2 Green MF, Kern RS, Heaton RK. Longitudinal studies of cognition and functional outcome in schizophrenia: implications for MATRICS. *Schizophr Res* 2004; **72**: 41–51.

3 Mucci A, Galderisi S, Gibertoni D, Rossi A, Rocca P, Bertolino A, et al. Factors associated with real-life functioning in persons with schizophrenia in a 4-year follow-up study of the Italian network for research on psychoses. *JAMA Psychiatry* 2021; **78**: 550–9.

4 Meier MH, Caspi A, Reichenberg A, Keefe RSE, Fisher H, Harrington H, et al. Neuropsychological decline in schizophrenia from the premorbid to post-onset period: evidence from a population-representative longitudinal study. *Am J Psychiatry* 2014; **171**: 91–101.

5 Woodberry KA, Giuliano AJ, Seidman LJ. Premorbid IQ in schizophrenia: a meta-analytic review. *Am J Psychiatry* 2008; **165**: 579–87.

6 Mesholam-Gately RI, Giuliano AJ, Goff KP, Faraone SV, Seidman LJ. Neurocognition in first-episode schizophrenia: a meta-analytic review. *Neuropsychology* 2009; **23**: 315–36.

7 Mollon J, David AS, Zammit S, Lewis G, Reichenberg A. Course of cognitive development from Infancy to early adulthood in the psychosis spectrum. *JAMA Psychiatry* 2018; **75**: 270–9.

8 Nuechterlein KH, Barch DM, Gold JM, Goldberg TE, Green MF, Heaton RK. Identification of separable cognitive factors in schizophrenia. *Schizophr Res* 2004; **72**: 29–39.

9 Sheffield JM, Karcher NR, Barch DM. Cognitive deficits in psychotic disorders: a lifespan perspective. *Neuropsychol Rev* 2018; **28**: 509–33.

10 Fioravanti M, Carlone O, Vitale B, Cinti ME, Clare L. A meta-analysis of cognitive deficits in adults with a diagnosis of schizophrenia. *Neuropsychol Rev* 2005; **15**: 73–95.

11 Fusar-Poli P, Deste G, Smieskova R, Barlati S, Yung AR, Howes O, et al. Cognitive functioning in prodromal psychosis: a meta-analysis. *Arch Gen Psychiatry* 2012; **69**: 562–71.

12 Heinrichs RW, Zakzanis KK. Neurocognitive deficit in schizophrenia: a quantitative review of the evidence. *Neuropsychology* 1998; **12**: 426–45.

13 Lewandowski KE, Cohen BM, Öngur D. Evolution of neuropsychological dysfunction during the course of schizophrenia and bipolar disorder. *Psychol Med* 2011; **41**: 225–41.

14 Birchwood M, Todd P, Jackson C. Early intervention in psychosis. the critical period hypothesis. *Br J Psychiatry Suppl* 1998; **172** (Suppl 3): 53–9.

15 de Winter L, Couwenbergh C, van Weeghel J, Hasson-Ohayon I, Vermeulen JM, Mulder CL, et al. Changes in social functioning over the course of psychotic disorders-a meta-analysis. *Schizophr Res* 2021; **239**: 55–82.

16 Luther L, Rosen C, Cummins JS, Sharma RP. The multidimensional construct of resilience across the psychosis spectrum: evidence of alterations in people with early and prolonged psychosis. *Psychiatr Rehabil J* 2020; **43**: 225–33.

17 Bora E, Murray RM. Meta-analysis of cognitive deficits in ultra-high risk to psychosis and first-episode psychosis: do the cognitive deficits progress over, or after, the onset of psychosis? *Schizophr Bull* 2014; **40**: 744–55.

18 Weinberger DR. Implications of normal brain development for the pathogenesis of schizophrenia. *Arch Gen Psychiatry* 1987; **44**: 660–9.

19 Murray RM, Bhavsar V, Tripoli G, Howes O. 30 years on: how the neurodevelopmental hypothesis of schizophrenia morphed into the developmental risk factor model of psychosis. *Schizophr Bull* 2017; **43**: 1190–6.

20 DeLisi LE, Sakuma M, Tew W, Kushner M, Hoff AL, Grimson R. Schizophrenia as a chronic active brain process: a study of progressive brain structural change subsequent to the onset of schizophrenia. *Psychiatry Res* 1997; **74**: 129–40.

21 Lieberman JA. Is schizophrenia a neurodegenerative disorder? A clinical and neurobiological perspective. *Biol Psychiatry* 1999; **46**: 729–39.

22 Haatveit B, Vaskinn A, Sundet KS, Jensen J, Andreassen OA, Melle I, et al. Stability of executive functions in first episode psychosis: one year follow up study. *Psychiatry Res* 2015; **228**: 475–81.

23 Kenney J, Anderson-Schmidt H, Scanlon C, Arndt S, Scherz E, McInerney S, et al. Cognitive course in first-episode psychosis and clinical correlates: a 4 year longitudinal study using the MATRICS consensus cognitive battery. *Schizophr Res* 2015; **169**: 101–8.

24 Torgalsbøen A-K, Mohn C, Rishovd Rund B. Neurocognitive predictors of remission of symptoms and social and role functioning in the early course of first-episode schizophrenia. *Psychiatry Res* 2014; **216**: 1–5.

25 González-Ortega I, de los Mozos V, Echeburúa E, Mezo M, Besga A, Ruiz de Azúa S, et al. Working memory as a predictor of negative symptoms and functional outcome in first episode psychosis. *Psychiatry Res* 2013; **206**: 8–16.

26 Sánchez-Torres AM, Moreno-Izco L, Lorente-Omeñaca R, Cabrera B, Lobo A, González-Pinto AM, et al. Individual trajectories of cognitive performance in first episode psychosis: a 2-year follow-up study. *Eur Arch Psychiatry Clin Neurosci* 2018; **268**: 699–711.

27 Cowman M, Holleran L, Lonergan E, O'Connor K, Birchwood M, Donohoe G. Cognitive predictors of social and occupational functioning in early psychosis: a systematic review and meta-analysis of cross-sectional and longitudinal data. *Schizophr Bull* 2021; **47**: 1243–53.

28 Fett A-KJ, Viechtbauer W, Dominguez M-G, Penn DL, van Os J, Krabbendam L. The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: a meta-analysis. *Neurosci Biobehav Rev* 2011; **35**: 573–88.

29 Vita A, Barlati S, Ceraso A, Nibbio G, Ariu C, Deste G, et al. Effectiveness, core elements, and moderators of response of cognitive remediation for schizophrenia: a systematic review and meta-analysis of randomized clinical trials. *JAMA Psychiatry* 2021; **78**: 848–58.

30 Wykes T, Huddy V, Cellard C, McGurk SR, Czobor P. A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. *Am J Psychiatry* 2011; **168**: 472–85.

31 Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021; **372**: n71.

32 Luchini C, Stubbs B, Solmi M, Veronese N. Assessing the quality of studies in meta-analyses: advantages and limitations of the Newcastle Ottawa Scale. *World Journal of Meta-Analysis* 2017; **5**(4): 80.

33 Viechtbauer W. Conducting meta-analyses in R with the metafor package. *J Stat Softw* 2010; **36**: 1–48.

34 Hedges LV. Distribution theory for glass's estimator of effect size and related estimators. *J Educ Stat* 1981; **6**: 107–28.

35 Dunlap WP, Cortina JM, Vaslow JB, Burke MJ. Meta-analysis of experiments with matched groups or repeated measures designs. *Psychol Methods* 1996; **1**: 170–7.

36 Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003; **327**: 557–60.

37 Zhou FC, Wang CY, Ungvari GS, Ng CH, Zhou Y, Zhang L, et al.et al. Longitudinal changes in prospective memory and their clinical correlates at 1-year follow-up in first-episode schizophrenia. *PLOS ONE* 2017; **12**(2): e0172114.

38 Lho SK, Kim M, Park J, Hwang WJ, Moon S-Y, Oh S, *et al*et al.. Progressive impairment of mismatch negativity is reflective of underlying pathophysiological changes in patients with first-episode psychosis. *Frontiers in Psychiatry* 2020; **11**: 8.

39 Peña J, Ojeda N, Segarra R, Eguiluz JI, García J, Gutiérrez M. Executive functioning correctly classified diagnoses in patients with first-episode psychosis: evidence from a 2-year longitudinal study. *Schizophrenia Research* 2011; **126** (1-3): 77–80.

40 Leeson V C, Barnes TRE, Hutton SB., Ron MA, Joyce EM.. IQ as a predictor of functional outcome in schizophrenia: a longitudinal, four-year study of first-episode psychosis. *Schizophrenia Research* 2009; **107**(1): 55–60.

41 Rund BR, Melle I, Friis S, Johannessen JO, Larsen TK, Midbøe LJ, et al.et al. The course of neurocognitive functioning in first-episode psychosis and its relation to premorbid adjustment, duration of untreated psychosis, and relapse. *Schizophrenia Research* 2007; **91**(1–3): 132–40.

42 Albus M, Hubmann W, Scherer J, Dreikorn B, Hecht S, Sobizack N, et al.et al. A prospective 2-year follow-up study of neurocognitive functioning in patients with first-episode schizophrenia. *European Archives of Psychiatry and Clinical Neuroscience* 2002; **252**(6): 262–7.

https://doi.org/10.1192/bjp.2022.131 Published online by Cambridge University Press

43 Chang WC, Hui CLM, Chan SKW, Lee EHM, Wong GHY, Chen EYH. Relationship between diminished expression and cognitive impairment in first-episode schizophrenia: a prospective three-year follow-up study. *Schizophrenia Research* 2014; **152**(1): 146–51.

44 Townsend LA, Norman RMG, Malla AK., Rychlo AD, Ahmed RR. Changes in cognitive functioning following comprehensive treatment for first episode patients with schizophrenia spectrum disorders. *Psychiatry Research* 2002; **113**(1-2): 69–81.

45 Lindgren M, Birling H, Kieseppä T, Tuulio-Henriksson A. Is cognitive performance associated with anxiety and depression in first-episode psychosis? *Journal of Affective Disorders* 2020; **263**: 221–7.

46 Nopoulos P, Flashman L, Flaum M, Arndt S, Andreasen N. Stability of cognitive functioning early in the course of schizophrenia. *Schizophrenia Research* 1994; **14**(1): 29–37.

47 Addington J, Saeedi H, Addington D. The course of cognitive functioning in first episode psychosis: changes over time and impact on outcome. *Schizophrenia Research* 2005; **78**(1): 35–43.

48 Higgins A, Lewandowski KE, Liukasemsarn S, Hall M-H. Longitudinal relationships between mismatch negativity, cognitive performance, and real-world functioning in early psychosis. *Schizophrenia Research* 2021; **228**: 385–93.

49 de Mello Ayres A, Scazufca M, Menezes PR, Nakano EY, Regina ACB, Schaufelberger MSet al.et al. Cognitive functioning in subjects with recent-onset psychosis from a low-middle-income environment: multiple-domain deficits and longitudinal evaluation. *Psychiatry Research* 2010; **179**(2): 157–64.

50 Liu CC, Hua MS, Hwang TJ, Chiu CY, Liu CM, Hsieh MH, et al. Neurocognitive functioning of subjects with putative pre-psychotic states and early psychosis. *Schizophrenia Research* 2015; **164**(1-3): 40–6.

51 Hoff AL, Svetina C, Shields G, Stewart J, DeLisi LE. Ten year longitudinal study of neuropsychological functioning subsequent to a first episode of schizophrenia. *Schizophr Res* 2005; **78**: 27–34.

52 Leeson VC, Barnes TRE, Hutton SB, Ron MA, Joyce EM. IQ as a predictor of functional outcome in schizophrenia: a longitudinal, four-year study of first-episode psychosis. *Schizophr Res* 2009; **107**: 55–60.

53 Mollon J, Reichenberg A. Cognitive development prior to onset of psychosis. *Psychol Med* 2018; **48**: 392–403.

54 Reichenberg A, Caspi A, Harrington H, Houts R, Keefe RSE, Murray RM, et al. Static and dynamic cognitive deficits in childhood preceding adult schizophrenia: a 30-year study. *Am J Psychiatry* 2010; **167**: 160–9.

55 Pantelis C, Yücel M, Bora E, Fornito A, Testa R, Brewer WJ, et al. Neurobiological markers of illness onset in psychosis and schizophrenia: the search for a moving target. *Neuropsychol Rev* 2009; **19**: 385–98.

56 Hawkins KA, Keefe RSE, Christensen BK, Addington J, Woods SW, Callahan J, et al. Neuropsychological course in the prodrome and first episode of psychosis: findings from the PRIME North America double blind treatment study. *Schizophr Res* 2008; **105**: 1–9.

57 Keefe RSE, Perkins DO, Gu H, Zipursky RB, Christensen BK, Lieberman JA. A longitudinal study of neurocognitive function in individuals at-risk for psychosis. *Schizophr Res* 2006; **88**: 26–35.

58 Harvey PD. When does cognitive decline occur in the period prior to the first episode of schizophrenia? *Psychiatry (Edgmont)* 2009; **6**: 12–4.

59 Zanelli J, Mollon J, Sandin S, Morgan C, Dazzan P, Pilecka I, et al. Cognitive change in schizophrenia and other psychoses in the decade following the first episode. *Am J Psychiatry* 2019; **176**: 811.

60 Fett A-KJ, Velthorst E, Reichenberg A, Ruggero CJ, Callahan JL, Fochtmann LJ, et al. Long-term changes in cognitive functioning in individuals with psychotic disorders: findings from the Suffolk County mental health project. *JAMA Psychiatry* 2020; **77**: 387–96.

61 Reichenberg A, Harvey PD. Neuropsychological impairments in schizophrenia: Integration of performance-based and brain imaging findings. *Psychol Bull* 2007; **133**: 833–58.

62 Albus M, Hubmann W, Mohr F, Tiedemann TV, Pechler S, Drießlein D, et al. Neurocognitive functioning in patients with first-episode schizophrenia: results of a prospective 15-year follow-up study. *Eur Arch Psychiatry Clin Neurosci* 2020; **270**: 689–98.

63 Bergh S, Hjorthøj C, Sørensen HJ, Fagerlund B, Austin S, Secher RG, et al. Predictors and longitudinal course of cognitive functioning in schizophrenia spectrum disorders, 10 years after baseline: the OPUS study. *Schizophr Res* 2016; **175**: 57–63.

64 Rund BR, Barder HE, Evensen J, Haahr U, Hegelstad WTV, Joa I, et al. Neurocognition and duration of psychosis: a 10-year follow-up of first-episode patients. *Schizophr Bull* 2016; **42**: 87–95.

65 Joshi YB, Thomas ML, Braff DL, Green MF, Gur RC, Gur RE, et al. Anticholinergic medication burden–associated cognitive impairment in schizophrenia. *AJP* 2021; **178**: 838–47.

66 Zipursky RB, Reilly TJ, Murray RM. The myth of schizophrenia as a progressive brain disease. *Schizophr Bull* 2013; **39**: 1363–72.

67 Bora E, Akdede BB, Alptekin K. The relationship between cognitive impairment in schizophrenia and metabolic syndrome: a systematic review and meta-analysis. *Psychol Med* 2017; **47**: 1030–40.

68 Stubbs B, Ku P-W, Chung M-S, Chen L-J. Relationship between objectively measured sedentary behavior and cognitive performance in patients with schizophrenia Vs controls. *Schizophr Bull* 2017; **43**: 566–74.

69 Joyce EM, Roiser JP. Cognitive heterogeneity in schizophrenia. *Curr Opin Psychiatry* 2007; **20**: 268–72.

70 O'Keeffe D, Hannigan A, Doyle R, Kinsella A, Sheridan A, Kelly A, et al. The iHOPE-20 study: relationships between and prospective predictors of remission, clinical recovery, personal recovery and resilience 20 years on from a first episode psychosis. *Aust N Z J Psychiatry* 2019; **53**: 1080–92.

71 Pantelis C, Wannan C, Bartholomeusz CF, Allott K, McGorry PD. Cognitive intervention in early psychosis - preserving abilities versus remediating deficits. *Curr Opin Behav Sci* 2015; **4**: 63–72.

72 Pinkham AE, Harvey PD, Penn DL. Social cognition psychometric evaluation: results of the final validation study. *Schizophr Bull* 2018; **44**: 737–48.

73 Mehta UM, Thirthalli J, Subbakrishna DK, Gangadhar BN, Eack SM, Keshavan MS. Social and neuro-cognition as distinct cognitive factors in schizophrenia: a systematic review. *Schizophr Res* 2013; **148**: 3–11.

74 Pinkham AE, Penn DL, Perkins DO, Lieberman J. Implications for the neural basis of social cognition for the study of schizophrenia. *AJP* 2003; **160**: 815–24.

75 Cuijpers P, Griffin JW, Furukawa TA. The lack of statistical power of subgroup analyses in meta-analyses: a cautionary note. *Epidemiol Psychiatr Sci* 2021; **30**: e78.

https://doi.org/10.1192/bjp.2022.131 Published online by Cambridge University Press