Cognitive trajectories following onset of psychosis: a meta-analysis

Andrew J. Watson, Lauren Harrison, Antonio Preti, Til Wykes and Matteo Cella

Background
Cognitive impairment is a core feature of schizophrenia, and is 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.

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, whereas others indicate cognitive stability or improvement across all domains. 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.

Support for a neurodevelopmental risk-factor model of schizophrenia, rather than a neurodegenerative model characterised by a chronic active illness progression, has a stronger relationship with social functioning than cognition. As in Bora & Murray (2014), this meta-analysis will include longitudinal studies examining cognitive changes within the proposed ‘critical period’ 1–5 years following psychosis onset.
when confounding effects of longer-term illness (such as medication) are likely to be minimised. 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.  

Method

Protocol and registration
This review follows the PRISMA guidelines for reporting systematic reviews. 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 ‘schizoa’ OR ‘FEP’ OR (‘first episode psychosis’) AND to identify cognitive measures: (‘Cog’, ‘neuropsych’, ‘neuropsych init’ OR ‘memory’ OR ‘attention’, OR ‘executive’ or ‘processing’ OR ‘social cog’, OR ‘social knowledge’ OR ‘attention bias’ OR ‘theory of mind’ OR (‘social perception’) AND to identify the study design: (‘longitudinal’ OR ‘follow-up’ OR ‘change’ 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.

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 baseline and follow-up scores. Where we computed a global cognitive 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 separate 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 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. 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). This approach is used to avoid the overestimation of the magnitude of effect in meta-analyses of longitudinal studies. 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.
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. $I^2$ 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. 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 ($n < 10$) meta-regression analyses were not performed. Studies including only age-adjusted scores, were not included when considering age as a moderator.

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 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

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.
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

| Domain                      | k | n     | Estimated effect (g) | 95% CI | Z    | P     | Q | Q (P) | R² | I²% | 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  | 0.65                 | 0.47-0.98 | 10.53 | <0.001 | 13.09 | 0.101 | 0.02 | 38.9 | 0.77     |
| Attention and vigilance     | 8 | 1140  | 0.65                 | 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                 | 0.36-0.84 | 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  | 0.006 | 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. R² quantifies the percentage of total variation across studies because of heterogeneity. Bias is the P-value of Egger’s test.
of Bora & Murray (2014)\textsuperscript{17} (0.02–0.31 in this analysis versus 0.13–0.38 in Bora & Murray\textsuperscript{15}). 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 verbal fluency. Greatest improvement was seen in executive functions. One possible explanation for this is that psychosis may lead to longer periods of restricted activity and opportunities for cognitive skill use, leading to a decline over time. Against this, others argue that cognitive worsening takes place during a prodromal period, with some studies showing evidence of cognitive worsening at this stage,\textsuperscript{13} while other studies found no evidence.\textsuperscript{56,57} Harvey\textsuperscript{38} 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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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\textsuperscript{62–64} with some evidence that any progression may be because of medication\textsuperscript{29,65,66} or lifestyle factors.\textsuperscript{67,68}

Further complexity in assessing cognition over time comes from individual heterogeneity,\textsuperscript{69} which may be obscured when assessing group means,\textsuperscript{26} as well as the potential for those who make good recoveries being underrepresented in studies with longer follow-up periods.\textsuperscript{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)\textsuperscript{17} analysis, highlighting

| Domain                          | k | n  | Estimated effect (g) | 95% CI            | Z   | P       | Q    | Q (p) | R² | F% | Bias (P) | Q[Q[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  | 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  | 0  | 0.37     |        |
| Working memory                  |   |     |                     |                   |     |         |      |       |    |    |          |        |
| Patients                        | 12| 844 | 0.15                | 0.02 to 0.28       | 2.32| <0.002  | 16.51| 0.24  | 0  | 0  | 0.84     | 0.02 (0.88) |
| Health controls                 | 9 | 537 | 0.16                | 0.05 to 0.28       | 2.71| <0.001  | 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  | 0  | 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  | 0  | 0.55     | –        |
| 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  | 0  | 0.37     | –        |
| Verbal fluency                  |   |     |                     |                   |     |         |      |       |    |    |          |        |
| Patients                        | 12| 997 | 0.11                | –0.01 to 0.23      | 1.76| 0.08    | 16.45| 0.13  | 0  | 33| 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  | –        |        |
| 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  | –        |        |
| Health controls                 | 3 | 232 | 0.22                | –0.18 to 0.62      | 1.09| 0.28    | 7.61 | 0.02  | 0  | 0  | 0.04     | 17        |
| Motor skills                    |   |     |                     |                   |     |         |      |       |    |    |          |        |
| Patients                        | 3 | 393 | 0.07                | –0.07 to 0.21      | 0.94| 0.35    | 0.10 | 0.95  | 0  | 0  | –        |        |
| Health controls                 |   |     |                     |                   |     |         |      |       |    |    |          |        |

a. Estimated effect (g) improvement in performance from first assessment to follow-up. Q is the measure of the heterogeneity of the distribution of effect size. \( P \) quantifies the percentage of total variation across studies due to heterogeneity. \( I^2 \) is the \( P \)-value of Egger's test. \( Q(bet) \) 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.
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 multiple time points. longitudinal and intervention studies measuring cognition at multiple time points. Satisfaction effects highlights the importance of including control samples in cognitive 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. 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.

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.

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 structures23 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,72 however, comparison of confidence intervals and careful interpretation do not change the conclusions of this analysis.

Data availability

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

Andrew J. Watson, Department of Psychology, Institute of Psychiatry, Psychology & Neuroscience, King’s College London, UK; and South London and Maudsley NHS Foundation Trust, London, UK; Lauren Harrison, Department of Psychology, Institute of Psychiatry, Psychology & Neuroscience, King’s College London, UK; Antonio Preti, Dipartimento di Neuroscienze, Università degli studi di Torino, Italy; and South London and Maudsley NHS Foundation Trust, London, UK; Matteo Celli, Department of Psychology, Institute of Psychiatry, Psychology & Neuroscience, King’s College London, UK; and South London and Maudsley NHS Foundation Trust, London, UK.

Correspondence: Andrew J. Watson. Email: andrew.j.watson@kcl.ac.uk

First received 21 Feb 2022, final revision 29 Jun 2022, accepted 25 Jul 2022

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. T1, baseline; T2, follow-up.

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.

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. Grouping social cognition constructs prohibits conclusions being made about these subdomains, particularly given the potential for their separate factor structures and neural bases. 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, however, comparison of confidence intervals and careful interpretation do not change the conclusions of this analysis.
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 from M.C. and A.P. All authors made significant contributions to drafting and/or revising the manuscript.

Funding

This research received no specific grant from any funding agency, commercial or not-for-profit sectors. T.W. acknowledges the support of the NIHR Maudsley Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King’s College London and the NHF-PGfAR RP-PG-0612-20002. The views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care.

Declaration of interest

None.

References

1. Green MF, Horan WP, Lee J. Non-social 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, Selidman LJ. Premorbid IQ in schizophrenia: a meta-analytic review. Am J Psychiatry 2008; 165: 579–67.
6. Mesholam-Gately RI, Giuliano AJ, Goff KP, Faraone SV, Seidman LJ. 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.
7. Molton I, David AS, Zammitt 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. Fusi-Poll P, Deste G, Smieleska 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, Zakinis KK. Neuropsychiatric deficit in schizophrenia: a quantitative review of the evidence. Neuropsychology 1998; 12: 426–45.
13. Lewandowski KE, Cohën BM, Öngür 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 Supp 1999; 172 (Supp 3): 53–9.
15. de Winter L, Cownenbergh 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, Cumnings 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, Bhavasar V, Tripoli G, Howes O. 30 years on: how the neuodevelopmental 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. Haavet HT, 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. Torgalsbee A-K, Mohn C, Rishovd Rund B. Neuropsychological 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; 269: 699–711.
27. Cowman M, Holleran L, Lonergan E, Churchill 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-K, 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, Desté 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 Newastle 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. 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. Uho SK, Kim M, Park J, Hwang WI, Moon S-Y, Oh S, 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, Gómez D, Jara C, 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): 77–87.
40. Leeson V, 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 L, et al. The course of neuropsychological 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, Hummbann W, Scherer J, Direkm B, Hecht S, Sobizak N, et al. A prospective 2-year follow-up study of neuropsychological functioning in patients with first-episode schizophrenia. European Archives of Psychiatry and Clinical Neuroscience 2002; 252(6): 262–7.
Addington J, Saeedi H, Addington D. The course of cognitive functioning in first-episode psychosis. Journal of Affective Disorders 2020; 263: 221–7.

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

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): 35–43.

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

de Mello Ayres A, Scacufca M, Menezes PR, Nakano YE, Regina ACP, Schaufelberger MS 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.

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.

Hoff AL, Svetina C, Shields G, Stewart J, DeLisi LE. Ten year longitudinal study of change in schizophrenia and other psychoses in the decade following the first episode of schizophrenia. Schizophr Res 2009; 107: 55–60.

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

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.

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

Hawkins KA, Keefe RSE, Christensen BK, Addington J, Woods SW, Calahan 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.

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.

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

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.

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

O’Keefe 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.

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

Mehta UM, Thiruthali 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.

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.

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: 678.