TECHNICAL COMMENTARY

Cognitive remediation

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Introduction

Cognitive impairment is a significant affliction for many people with schizophrenia, and affects domains including executive function, attention, memory (particularly verbal memory), and social cognition[1-3]. These deficits interfere considerably with day-to-day function. Cognitive remediation (or rehabilitation) interventions usually take the form of repetitive exercises (with or without computers and sometimes augmented by group sessions, strategy coaching and homework exercises) which serve as training for cognitive processes such as memory or attention, as well as social skills and communication[4-10]. Strategy learning focuses on providing alternative strategies to compensate for the observed difficulties with cognition; in contrast, rehearsal learning is aimed at restitution of lost skills. This type of intervention is specifically targeted to particular cognitive domains which are known to be deficient in people with schizophrenia, with the intention of compensating or improving functional outcome[11].

Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2000 that report results separately for people with a diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder or first episode schizophrenia. Reviews were identified by searching the databases MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO and the Cochrane library. Hand searching reference lists of identified reviews was also conducted. When multiple copies of reviews were found, only the most recent version was included. Reviews with pooled results were given priority for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis[12]. Reviews rated as having less than 50% of items checked have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach[13] where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention, or other matter under review, are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large or if there is a dose dependent response. We have also taken into account sample size and whether results are consistent, precise and direct with low associated risks (see end of table for an explanation of these terms). The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

Results

We found thirteen systematic reviews that met our inclusion criteria[4-11, 14-18].

- Moderate to high quality evidence suggests a medium-sized benefit of cognitive remediation over control interventions for improving attention, memory, processing speed, social function, problem solving, and a small benefit for symptoms.
- Moderate to low quality evidence suggests similar level of effectiveness for both short and long duration of intervention, and that strategy-focused learning may be more generally effective than rehearsal learning for training cognitive skills.
- Moderate to low quality evidence suggests automated training programs (focused on rehearsal learning) may improve vigilance, arithmetic and visuospatial processing, with computer-based automated paradigms improving reaction time, problem solving and memory. Strategy-based training paradigms may be beneficial for attention, working memory, and planning, but the benefit of strategy coaching in conjunction with computer-based task practice is unclear. Environmental intervention to reduce cognitive demands may improve illness severity and motivation levels.

Anaya C, Aran AM, Ayuso-Mateos JL, Wykes T, Vieta E, Scott J

A systematic review of cognitive remediation for schizo-affective and affective disorders

Journal of Affective Disorders 2012; 142: 13-21

View review abstract online

Comparison	**Cognitive remediation interventions vs. a control condition or a placebo intervention (such as computer literacy training). The duration of total time ranged from 6 to 100 hours.** **Studies predominately included people with schizophrenia, schizophreniform, or schizoaffective disorders. Some studies included people with affective disorders.**
Summary of evidence	**Moderate to high quality evidence (consistent, precise, indirect, large samples) suggests cognitive remediation provided significant, small to medium-sized benefit for improving cognitive skills.**
Global cognition	
A small to medium-sized benefit of cognitive remediation for neuropsychological performance over control conditions; 18 studies (mixed design), N = 881, d = 0.36, 95%CI 0.24 to 0.45, $p < 0.01$, Q = 33.94, $p < 0.01$ *After removing two outliers, the effect was similar and results were reported as being homogenous;* 16 studies, d = 0.32, 95%CI 0.20 to 0.43, $p < 0.01$ *A larger effect was reported in the sub-group analysis of randomised trials only;* 8 RCTs, N = 553, d = 0.41, 95%CI 0.30 to 0.51, $p < 0.01$, Q-test $p > 0.05$	
Consistency in results‡	Consistent after removal of outliers.
Precision in results§	Precise
Directness of results‖	Indirect comparison (mixed control conditions are combined).

Grynszpan O, Perbal S, Pelissolo A, Fossanti P, Jouvent R, Dubal S, Perez-Diaz F

Efficacy and specificity of computer-assisted cognitive remediation in

schizophrenia: a meta-analytical study

Psychological Medicine 2011; 41: 163-173

View review abstract online

Comparison	**Computer-based cognitive rehabilitation interventions vs. a control condition or a placebo intervention (such as computer literacy training). The number of sessions ranged from 6 to 104.**
Summary of evidence	**Moderate to high quality evidence (mostly consistent, precise, indirect, large samples) suggests computerised cognitive remediation provides significant, small to medium-sized benefit over control interventions for improving cognitive skills.**

Global cognition

17 trials, N = 805, compared computerised cognitive remediation to control conditions for improving skills in neuropsychological performance or emotion recognition. Cognitive tasks mostly included training for processing speed, memory, attention, or problem solving.

The overall effect from all studies showed a small to medium size benefit of cognitive remediation over control conditions;

17 studies, d = 0.38, 95%CI 0.20 to 0.55, $p < 0.001$, Q = 20.13, p = 0.21

In specific cognitive domains, remediation showed a significant benefit for;

Speed of processing: 9 studies, d = 0.36, 95%CI 0.07 to 0.65, p = 0.02, Q = 14.34, p = 0.07

Attention/vigilance: 6 studies, d = 0.29, 95%CI 0.09 to 0.49, p = 0.01, Q = 2.30, p = 0.81

Working memory: 8 studies, d = 0.29, 95%CI 0.10 to 0.47, p = 0.008, Q = 4.72, p = 0.69

Verbal Learning and memory: 12 studies, d = 0.30, 95%CI 0.03 to 0.58, p = 0.03, Q = 25.93, p = 0.007

Social cognition: 6 studies, d =0.64, 95%CI 0.29 to 0.99, p = 0.005, Q = 8.33, p = 0.14

No significant benefit of remediation was found for;

Visual learning and memory: 3 studies, d = -0.09, 95%CI -1.29 to 1.11, p = 0.77, Q = 6.72, p = 0.03

Reasoning and problem solving: 7 studies, d = 0.48 95%CI -0.15 to 1.10, p = 0.11, Q = 34.50, p <0.001

Consistency in results	Mostly consistent.
Precision in results	Mostly precise, except for visual learning and problem solving.
Directness of results	Indirect comparison (mixed control conditions are combined).

Kluwe-Schiavon B, Sanvicente-Vieira B, Kristensen CH, Grassi-Oliveira R

Executive functions rehabilitation for schizophrenia: a critical systematic review

Journal of Psychiatric Research 2013; 47: 91-104

View review abstract online

Comparison	**Cognitive rehabilitation interventions (both computerised and pen/paper) vs. a control condition, treatment duration ranging from 0.5-12 hours per week, over 3-48 weeks (average 23 weeks).**
Summary of evidence	**Moderate to low quality evidence (direct, unable to assess consistency or precision) suggests cognitive remediation provided significant, small benefit over control interventions for training executive function skills.**

Global cognition

30 trials, N = 805, compared cognitive remediation to control, for improving skills in executive functioning directly, or indirectly through training processing speed, memory, or attention.

Computerised cognitive remediation

Compared to a wait-list control, 1 study found benefits for improving attention, memory, logic thought, reasoning and executive function tasks, however a second study found no differences to the control condition.

Compared to treatment as usual, 2 studies found benefits of cognitive remediation for autonomy, memory, word fluency and comprehension and 2 additional studies found improved quality of life.

Compared to placebo (computer game), 2 studies found cognitive remediation benefits for verbal learning and global cognition but 1 study found no difference.

Only 5 of 8 studies found that the benefits of cognitive remediation were maintained at 6 months post-treatment.

3 studies compared computerized cognitive remediation plus pen/paper cognitive remediation to pen/paper alone, and found the computerized intervention had greater benefits that were sustained for longer periods post-treatment.

General computer stimulation (not cognitive remediation specific) was also associated with improvements in general cognition, autonomy and problem solving in 3 studies.

Pen and paper cognitive remediation

Compared to treatment as usual, 6 studies found benefits of cognitive remediation for social function, executive function, processing speed, word fluency, memory, and perception. 1 study found greater difference in the control group (multi-disciplinary day treatment).

1 study found significant benefits of cognitive remediation over Cognitive Behavioural Therapy for

symptom severity (PANSS scores). *Vocational training* 5 studies of vocational training found significant improvements in executive function, which were maintained at 6 month follow up.	
Consistency in results	No measure of consistency is reported.
Precision in results	No measure of precision is reported.
Directness of results	Direct

Krabbendam L, Aleman A

Cognitive rehabilitation in schizophrenia: a quantitative analysis of controlled studies

Psychopharmacology 2003; 169(3-4): 376-82

View review abstract online

Comparison	**Cognitive rehabilitation interventions vs. a control condition (a placebo intervention, another intervention, or standard treatment) for increasing trained skills.**
Summary of evidence	**Moderate to high quality evidence (consistent, precise, indirect, large samples) suggests cognitive remediation provided significant medium benefit over control interventions for training cognitive skills. Moderate to low quality evidence (imprecise) suggests both short and long duration of intervention had the same effectiveness, and that strategy learning may be more effective than rehearsal learning.**
Global cognition	
12 trials (10 randomised), N = 543, compared cognitive remediation to control intervention for improving skills for the task in question. The number of sessions ranged from 1 to 78. Tasks mostly included computer exercises for different cognitive domains such as attention and vigilance training, memory training, problem solving, executive function, but also included WCST training. *The overall effect from all studies showed a medium effect size suggesting benefit of cognitive remediation over control conditions;* d = 0.45, 95%CI 0.26 to 0.64, p not reported, Q_W = 14.3, p = 0.43	

Subgroup analysis: duration of training *A medium-sized effect suggests a benefit of cognitive remediation over control, regardless of the number of sessions;* 5 studies considered a cognitive remediation intervention with less than 15 sessions (mean = 7.7 sessions). *d* = 0.44, 95%CI 0.01 to 0.85, *p* not reported 6 studies considered 15 or more sessions (mean = 33 sessions). *d* = 0.45, 95%CI 0.18 to 0.85, *p* not reported Q_B = 0.001, *p* = 0.978
Subgroup analysis: type of training *Small to medium-sized effects suggest a slightly (non-significantly) greater benefit of strategy learning cognitive remediation over rehearsal learning cognitive remediation, compared to control conditions;* 6 studies considered a cognitive remediation intervention with rehearsal learning, showing medium size effect over control conditions. *d* = 0.34, 95%CI -0.03 to 0.70, *p* not reported 7 studies considered a cognitive remediation intervention with strategy learning, showing medium size effect over control conditions. *d* = 0.52, 95%CI 0.25 to 0.78, *p* not reported Q_B = 0.95, *p* = 0.36

Consistency in results	Consistent
Precision in results	Precise
Directness of results	Indirect comparison (mixed control conditions are combined).

Kurtz MM, Moberg PJ, Gur RC, Gur RE

Approaches to cognitive remediation of neuropsychological deficits in schizophrenia: a review and meta-analysis

Neuropsychology Review 2001; 11(4): 197-210

View review abstract online

Comparison	**Cognitive rehabilitation interventions vs. no treatment, a placebo intervention, or standard treatment for improving**

	executive functioning.
Summary of evidence	**Moderate to high quality evidence (consistent, precise, indirect, medium samples) suggests a large effect size benefit of expanded remediation instructions for improving cognitive flexibility measures assessed by Wisconsin Card Sorting Test (WCST).**
Cognitive flexibility	
11 studies (number of studies randomised not reported) with 181 patients (control N not reported) assessed remediation techniques (mostly 1 day) for improving WCST scores. Intervention generally involved expanded instructions. *Results suggest a large effect of remediation on cognitive flexibility compared to control conditions* Overall results immediately after training 11 studies, d = 0.98, 95%CI 0.80 to 1.16, p not reported, Q_W = 17.6, p = 0.61 WCST: Categories 9 studies, d = 1.08, 95%CI 0.80 to 1.37, p not reported, Q_W = 5.80 p not reported WCST: Perseverative errors 8 studies, d = 0.93, 95%CI 0.64 to 1.21, p not reported, Q_W = 9.10 p not reported WCST: Conceptual learning 4 studies, d = 0.90, 95%CI 0.52 to 1.28, p not reported, Q_W = 1.95 p not reported Q_B = 0.79, p = 0.68 - no significant differences in results between the three sub-domains above	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Indirect comparison (mixed control conditions are combined).

McGrath JJ, Hayes RL

Cognitive rehabilitation for people with schizophrenia and related conditions

Cochrane Database of Systematic Reviews 2000; 3: CD000968

View review abstract online

Comparison 1	**Cognitive rehabilitation interventions (including computer) vs. a**

	placebo cognitive procedure.
Summary of evidence	**Moderate to low quality evidence (consistent, imprecise, direct, small samples) suggests no difference between cognitive remediation and placebo for study retention.** **Low quality evidence (unable to assess consistency or precision, small sample size) is unclear as to any benefit of cognitive remediation over placebo for improving attention, memory or mental state.**
Mental state: Brief Psychiatric Rating Scale	
No significant difference between groups; 1 RCT (N = 54), MD = -0.90, 95%CI -2.93 to 1.13, *p* = 0.38	
Leaving the study early	
No significant difference between groups; 2 RCTs (N = 84), OR = 1.01, 95%CI 0.19 to 5.33, *p* = 1.00, Q_W = 0.0, *p* = 1.0, I^2 = 0%	
Attention: Continuous Performance Test	
No significant differences between groups; Correct letter detection: 1 RCT (N = 54), MD = 6.60, 95%CI -11.67 to 24.87, *p* = 0.48 Total percent correct: 1 RCT (N = 54), MD = 3.20, 95%CI -6.04 to 12.44, *p* = 0.50 No differences in results between correct letter detection and total correct (Q_B = 0.11, *p* = 0.74)	
Memory: Weschler Memory Scale-Revised	
No significant differences between groups; Logical memory, immediate: One RCT (N = 24), MD = 7.30, 95%CI -3.58 to 18.18, *p* = 0.19 Logical memory, delayed: One RCT (N = 24), MD = 8.40, 95%CI -1.04 to 17.84, *p* = 0.08 No differences in results between immediate and delayed logical memory (Q_B = 0.02, *p* = 0.88) *A trend effect for visual memory favoured placebo;* Visual memory, immediate: One RCT (N = 24), MD = 9.50, 95%CI -8.31 to 27.31, p = 0.30 Visual memory, delayed: One RCT (N = 24), MD = 15.30, 95%CI -0.04 to 30.64, *p* = 0.051 No differences in results between immediate and delayed visual memory (Q_B = 0.23, *p* = 0.63)	
Comparison 2	**Cognitive rehabilitation interventions vs. occupational therapy for increasing trained skills.**
Summary of evidence	**Low quality evidence (unable to assess consistency or**

	precision, small sample size) is unclear as to any benefit of cognitive remediation over occupational therapy for improving study retention, self-esteem, memory, mental state, cognitive flexibility, or planning skills. Effect size trends (from single RCTs) suggest most outcomes favoured occupational therapy.
Mental state: Brief Psychiatric Rating Scale	
No significant difference between groups; 1 RCT (N = 30), MD = -2.50, 95% CI -10.64 to 5.64, *p* = 0.55	
Leaving the study early	
No significant difference between groups; 1 RCT (N = 33), OR = 3.21, 95%CI 0.30 to 34.64, *p* = 0.34	
Self-esteem: Rosenberg scale	
Self-esteem ratings favoured occupational therapy 1 RCT (N = 29), MD = 6.30, 95%CI 1.07 to 11.53, *p* = 0.018	
Cognitive flexibility: Stroop test	
No significant differences between groups; Oral word fluency: 1 RCT (N = 30), MD = -3.30, 95%CI -12.68 to 6.08, *p* = 0.49 Stroop screening test: 1 RCT (N = 30), MD = 4.80, 95%CI -9.88 to 19.48, *p* = 0.52 No differences in results between tasks (Q_B = 0.83, *p* = 0.36)	
Memory: Weschler Memory Scale-Revised	
No significant differences between groups; Sentence span: 1 RCT (N = 24), MD = 0.10, 95%CI -0.74 to 0.94, *p* = 0.82 Visual span: 1 RCT (N = 24), MD = -0.10, 95%CI -1.51 to 1.31, *p* = 0.89 No differences in results between these two tasks (QB = 0.06, p = 0.81) Dual span: 1 RCT (N = 24), MD = 9.90, 95%CI -2.74 to 22.54, *p* = 0.12 Digit span: 1 RCT (N = 24), MD = 0.40, 95%CI-1.85 to 2.65, *p* = 0.73	
Planning: Tower of London test	
A trend effect favouring occupational therapy; 1 RCT (N = 30), MD = 1.00, 95%CI 0.00 to 2.00, *p* = 0.051	
Consistency in results	Not applicable, one RCT per outcome.

Precision in results	Imprecise for study attrition, unable to assess other outcomes.
Directness of results	Direct

McGurk SR, Twamley EW, Sitzer DI, McHugo GJ, Mueser KT

A meta-analysis of cognitive remediation in schizophrenia

American Journal of Psychiatry 2007; 164(12): 1791-802

View review abstract online

Comparison	**Cognitive rehabilitation interventions vs. a control condition (either passive or active control) for increasing trained skills.**
Summary of evidence	**Moderate to high quality evidence (consistent, precise, indirect, large samples) suggests cognitive remediation provided medium effect size benefit over control conditions for improving attention, processing speed, problem solving, and social cognition, and small benefit for symptoms. Moderate quality evidence (inconsistent) suggests cognitive remediation provided medium effect size benefit over control interventions for improving verbal working memory and a small benefit for general functioning but no benefit for visual learning and visual memory.**

Global cognition

26 RCTs, compared cognitive remediation to control conditions. Tasks included both computerised and non-computerised training for attention and abstraction.

The results show a significant, medium effect size benefit favouring cognitive remediation over control conditions for global cognition immediately post-treatment;

All studies, N = 1214, d = 0.41, 95%CI 0.29 to 0.52, $p < 0.001$, $Q_W = 35.3$, p = NS

Subgroup analysis of studies reporting results immediately post-treatment and follow up (8 months) show a significant, medium-sized effect favouring cognitive remediation over control conditions both immediately post-treatment and at follow up;

Post-treatment: d = 0.56 95%CI 0.33 to 0.79, p <0.001, Q_W = 3.4, p = NS

Follow-up (average 8 months): d = 0.66 95%CI 0.43 to 0.89, p <0.001, Q_W =7 .8, p = NS

Cognitive domains

Subgroup analyses for cognitive domains *Significant, medium-sized effect of improved attention/vigilance over control conditions;* Number of studies not reported, N = 659, *d* = 0.41, 95%CI 0.25 to 0.57, *p* < 0.001, Q_W = 9.8, *p* = NS *Significant, medium-sized effect of improved processing speed over control conditions;* Number of studies not reported, N = 655, *d* = 0.48, 95%CI 0.28 to 0.69, *p* < 0.001, Q_W = 20.7, *p* = NS *Significant, medium-sized effect of improved verbal working memory over control conditions;* N = 428, *d* = 0.52, 95%CI 0.33 to 0.72, *p* < 0.001, Q_W = 3.9, *p* = NS *Significant, small to medium-sized effect of improved verbal learning and memory over control conditions;* N = 858, *d* = 0.39, 95%CI 0.20 to 0.58, *p* < 0.001, Q_W = 26.6, *p* < 0.05 *No significant differences in visual learning and memory;* N = 424, *d* = 0.09, 95%CI -0.26 to 0.43, *p* = NS, Q_W = 14.5, *p* < 0.05 *Significant, medium-sized effect of improved reasoning and problem solving over control conditions;* N = 564, *d* = 0.47, 95%CI 0.30 to 0.64, *p* < 0.001, Q_W = 21.8, *p* = NS *Significant, medium-sized effect of improved social cognition over control conditions;* N = 228, *d* = 0.54, 95%CI 0.22 to 0.88, *p* < 0.001, Q_W = 2.8, *p* = NS
Symptoms and functioning
Significant, small effect of improved symptoms over control conditions; N = 709, *d* = 0.28, 95%CI 0.13 to 0.43, *p* < 0.001, Q_W = 12.2, *p* = NS *Significant, small to medium-sized effect of improved functioning over control conditions;* N = 615, *d* = 0.35, 95%CI 0.07 to 0.62, *p* < 0.05, Q_W = 25.7, *p* < 0.01

Consistency in results	Consistent for all except verbal and visual learning and memory, and functioning.
Precision in results	Precise
Directness of results	Indirect comparisons (mixed control conditions are combined).

Pfammatter M, Junghan UM, Brenner HD

Efficacy of psychological therapy in schizophrenia: conclusions from meta-analyses

Schizophrenia Bulletin 2006; 32(Suppl 1): S64-80

View review abstract online

Comparison	**Cognitive rehabilitation interventions vs. a control condition (undefined) for increasing trained skills.**
Summary of evidence	**Moderate to high quality evidence (consistent, precise, indirect, large samples) suggests cognitive remediation provides a small to medium-sized effect over controls for improving attention, memory, executive function, social cognition, symptom severity, and social functioning.**
Cognitive domains	
19 RCTs were included that investigated cognitive remediation with varying control groups. *Small to medium effect size for improving attention over control conditions;* 13 RCTs, N = 539, *g* = 0.32, 95%CI 0.15 to 0.49, *p* not reported, Q_W = 7.67, *p* = 0.81 *Small to medium effect size for improving memory over control conditions;* 12 RCTs, N = 704, *g* = 0.36, 95%CI 0.20 to 0.51, *p* not reported, Q_W = 15.77, *p* = 0.17 *Small effect size for improving executive functioning over control conditions;* 10 RCTs, N = 606, *g* = 0.28, 95%CI 0.12 to 0.40, *p* not reported, Q_W = 6.24, *p* = 0.72 *Small to medium effect size for improving social cognition over control conditions;* 3 RCTs, N = 228, *g* = 0.40, 95%CI 0.13 to 0.68, *p* not reported, Q_W = 0.28, *p* = 0.87 *Medium effect size for improving social functioning over control conditions;* 7 RCTs, N = 306, *g* = 0.49, 95%CI 0.27 to 0.70, *p* not reported, Q_W = 10.82, *p* = 0.09 *Small effect size for improving general psychopathology over control conditions;* 9 RCTs, N = 452, *g* = 0.20, 95%CI 0.01 to 0.38, *p* not reported, Q_W = 5.01, *p* = 0.76 *Small effect size for improving negative symptoms over control conditions;* 9 RCTs, N = 394, *g* = 0.24, 95%CI 0.04 to 0.44, *p* not reported, Q_W = 13.52, *p* = 0.09	
Consistency in results	Consistent
Precision in results	Mostly precise

Directness of results	Indirect comparisons (mixed control comparisons combined).

Pilling S, Pebbington P, Kuipers P, Garety P, Geddes J, Martindale B, Orbach G, Morgan C

Psychological treatments in schizophrenia: II. Meta-analyses of randomized controlled trials of social skills training and cognitive remediation

Psychological Medicine 2002; 32(5): 783-91

View review abstract online

Comparison	**Cognitive remediation interventions vs. a control condition (undefined) for increasing trained skills.**
Summary of evidence	**Low quality evidence (imprecise, indirect, small sample) suggests no significant benefit of cognitive remediation over control conditions for attention, verbal memory, visual memory, mental state, planning or cognitive flexibility.**

Cognitive domains

5 studies (total N = 170) compared cognitive remediation with varying control groups.

No significant differences were reported between cognitive remediation and control conditions for attention, verbal memory, visual memory, mental state, planning or cognitive flexibility;

Attention

2 RCTs, N = 87, OR = 0.11, 95%CI -0.31 to 0.53, *p, Q* not reported

Verbal memory

4 RCTs, N = 117, OR = 0.14, 95%CI -0.23 to 0.50, *p, Q* not reported

Visual memory

2 RCTs, N = 48, OR = 0.35, 95%CI -0.46 to 1.16, *p, Q* not reported

Mental state

2 RCTs, N = 84, OR = -0.23, 95%CI -0.66 to 0.20, *p, Q* not reported

Planning

1 RCT, N = 24, OR = 0.21, 95%CI -0.49 to 0.92, *p* not reported

Cognitive flexibility

1 RCT, N = 30, OR = 0.23, 95%CI -0.49 to 0.95, *p* not reported	
Consistency in results	No measures of heterogeneity reported but authors state consistency.
Precision in results	Imprecise
Directness of results	Indirect (mixed control conditions combined).

Suslow T, Schonauer K, Arolt V

Attention training in the cognitive rehabilitation of schizophrenic patients: a review of efficacy studies

Acta Psychiatrica Scandinavica 2001; 103(1): 15-23

View review abstract online

Comparison	**Cognitive rehabilitation interventions (training duration 3-12 weeks, median 18 sessions) vs. a control condition (no treatment, a placebo intervention, or standard treatment) for improving attention.**
Summary of evidence	**Low quality evidence (unable to assess consistency or precision, indirect, small sample) is unclear about the effectiveness of cognitive remediation interventions for improving attention.**
Attention	
9 studies, N ranging from 10 to 40 (total N not reported) Generally, results showed no overall effect of cognitive remediation for measures of attention including error score and sustained attention in attention stress tests, reaction time (latency, speed and accuracy) and mental arithmetic, labyrinth test, search-a-word, trail making and Stroop tests. Authors state that there was greater improvement was reported in the cognitive remediation group compared to the control group for measures of attention including total score in attention stress tests, word recognition, Stroop interference, both Wechsler memory and trail making tests, right and wrong letter detection.	
Consistency in results	No measure of consistency is reported.
Precision in results	No measure of precision is reported.

Directness of results	Indirect comparison (mixed control conditions)

Turner DT, van der Gaag M, Karyotaki E, Cuijpers P

Psychological Interventions for Psychosis: A Meta-Analysis of Comparative Outcome Studies

American Journal of Psychiatry 2014; 171: 523-538

View review abstract online

Comparison	**Cognitive remediation (training duration 3 weeks to 2 years) vs. any other psychosocial intervention for symptoms.**
Summary of evidence	**Moderate to high quality evidence (consistent, precise, indirect, large samples) suggests a small effect of improved overall symptoms with cognitive remediation when compared to other psychosocial interventions, but not when positive and negative symptoms were assessed separately.**

Symptoms

Improved overall symptoms in people receiving cognitive remediation compared to controls in the analysis excluding 1 study with a high risk of bias;

11 RCTs, N ~917, g = 0.13, 95%CI -0.05 to 0.31, $p > 0.05$, $I^2 = 31.69\%$, $p > 0.05$

Excluding RCTs with a high risk of bias: 10 RCTs, g = 0.20, 95%CI 0.01 to 0.39, $p < 0.05$, $I^2 = 20.65\%$, $p > 0.05$

Excluding RCTs with a low risk of bias: 6 RCTs, g = 0.14 , 95%CI -0.05 to 0.33, $p > 0.05$, $I^2 = 0\%$, $p > 0.05$

Excluding RCTs with any risk of bias: 4 RCTs, g = 0.12, 95%CI -0.11 to 0.34, $p > 0.05$, $I^2 = 0\%$, $p > 0.05$

No significant differences between groups in positive symptoms;

6 RCTs, g = 0.16, 95%CI -0.17 to 0.49, $p > 0.05$, $I^2 = 64.56\%$, $p < 0.05$

Excluding RCTs with a low risk of bias: 4 RCTs, g = 0.29, 95%CI -0.06 to 0.64, $p > 0.05$, $I^2 = 54.59\%$, $p > 0.05$

No significant differences between groups in negative symptoms;

6 RCTs, g = -0.14 , 95%CI -0.39 to 0.06, $p > 0.05$, $I^2 = 40.99\%$, $p > 0.05$

Excluding RCTs with high or low risk of bias: 4 RCTs, g = -0.08 , 95%CI -0.38 to 0.22, $p > 0.05$, $I^2 = 42.59\%$, $p > 0.05$

Consistency in results	Consistent for all analyses apart from positive symptoms.
Precision in results	Precise
Directness of results	Indirect comparison (mixed control conditions combined).

Twamley EW, Jeste DV, Bellack AS

A review of cognitive training in schizophrenia

Schizophrenia Bulletin 2003; 29(2): 359-82

View review abstract online

Comparison	**Cognitive training sessions (duration range 20 to 60 minutes, 1 day to 9 months) that generalize to all cognitive domains vs. a control condition (no treatment, treatment as usual, attention placebo, or a training placebo).**
Summary of evidence	**Moderate to low quality evidence (indirect, large sample, unable to assess consistency or precision) suggests automated training paradigms may improve vigilance, arithmetic and visuospatial processing, with computer-based automated paradigms improving reaction time, problem solving and memory. Strategy-based training paradigms may be beneficial for attention, working memory, planning, but the benefit of strategy coaching in conjunction with computer-based task practice is unclear. Environmental intervention to decrease cognitive demands may improve illness severity and motivation levels.**

Cognitive domains

17 studies, N = 695, compared cognitive training (CT) with control conditions (passive or active). Tasks were either drill- or strategy-oriented approaches, administered with or without a computer.

14 of 17 studies report statistically significant differences favouring CT over control in at least one cognitive domain.

CT was associated with:

Improvements in neuropsychological performance, d = 0.32, 95%CI, p not reported

Reductions in symptom severity, d = 0.26, 95%CI, p not reported

Improvements in everyday function, d = 0.51, 95%CI, p not reported

Subgroup analyses: task-specific comparison Automated drill-oriented approach, *d* = 0.42 95%CI, *p* not reported. 2 of 3 studies reported positive effects of CT for improving vigilance, arithmetic, abstraction and visuospatial ability. Strategy-oriented approach, *d* = 0.23 95%CI, *p* not reported. 4 of 4 studies report positive effect of CT for improving attention, working memory, planning, and social cue recognition. Computer assisted automated drill-oriented approach, *d* = 0.49 95%CI, *p* not reported. 6 of 8 studies report positive effect of CT for improving reaction time, problem solving, working and long term memory, psychiatric symptoms. Computer assisted strategy-oriented approach, *d* = -0.38 for memory training 95%CI, *p* not reported. One study reported no improvements in patients trained for memory, but some improvement in patients trained for problem solving. Environmental intervention (cognitive adaptation training), *d* = 1.22 95%CI, *p* not reported. One study reported improvements in symptom levels, motivation, global function and re-hospitalisation rates.	
Consistency in results	No measure of consistency is reported.
Precision in results	No measure of precision is reported.
Directness of results	Indirect (mixed control conditions combined).

Wykes T, Huddy V, Cellard C, McGurk SR, Czobor P

A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes

American Journal of Psychiatry 2011; 168(5): 472-85

View review abstract online

Comparison	**Cognitive rehabilitation interventions vs. a control condition for improving global cognitive ability.**
Summary of evidence	**Moderate quality evidence (precise, indirect, mostly inconsistent) suggests a medium benefit of cognitive remediation for improving global cognitive functioning, with benefits reported for attention, speed, memory, reasoning, social function, as well as small improvements in symptoms and global functioning. Global cognitive and global functioning improvements were sustained at follow-up.**

Cognitive domains
40 studies, N = 2104, compared cognitive remediation with control conditions.
Cognitive remediation showed significant, medium size benefits over control conditions for improving global cognition;
38 studies, N = 1982, d = 0.448, 95%CI 0.306 to 0.590, $p < 0.05$, $Q_W = 76.18$, $p < 0.001$
Small to medium size benefits were also found when individual cognitive domains were assessed;
Attention: 16 studies, N = 901, d = 0.250, 95%CI 0.080 to 0.419, $p < 0.05$, $Q_W = 19.47$, $p = 0.19$
Processing speed: 24 studies, N = 1332, d = 0.258, 95%CI 0.072 to 0.445, $p < 0.05$, $Q_W = 52.64$, $p < 0.0001$
Verbal working memory: 20 studies, N = 1029, d = 0.346, 95%CI 0.186 to 0.506, $p < 0.05$, $Q_W = 25.69$ $p = 0.14$
Verbal learning: 23 studies, N = 1346, d = 0.410, 95%CI 0.273 to 0.548, $p < 0.05$, $Q_W = 29.24$, $p = 0.14$
Problem solving: 25 studies, N = 1389, d = 0.572, 95%CI 0.222 to 0.922, $p < 0.05$, $Q_W = 203.25$, $p < 0.001$
Social cognition: 7 studies, N = 539, d = 0.651, 95%CI 0.331 to 0.972, $p < 0.05$, $Q_W = 15.41$ $p = 0.03$
Significant small benefits were also reported for additional outcomes;
Symptom severity: 20 studies, N = 1114, d = 0.177, 95%CI 0.034 to 0.321, $p < 0.05$, $Q_W = 23.50$, $p = 0.22$
Global functioning: 19 studies, N = 1036, d = 0.418, 95%CI 0.216 to 0.620, $p < 0.05$, $Q_W = 39.35$, $p = 0.003$
No benefit was found for visual learning:
10 studies, N = 547, d = 0.150, 95%CI -0.077 to 0.377, $p > 0.05$, $Q_W = 13.37$, $p = 0.05$
At follow up, significant benefits remained for global cognition and global functioning, but not for symptom severity;
Global cognition: 11 studies, N = 731, d = 0.428, 95%CI 0.184 to 0.671, $p < 0.05$, $Q_W = 17.27$, $p = 0.07$
Global functioning: 12 studies, N = 745, d = 0.372, 95%CI 0.110 to 0.635, $p < 0.05$, $Q_W = 25.72$, $p = 0.005$
Symptom severity: 8 studies, N = 527, d = 0.174, 95%CI -0.031 to 0.481, $p > 0.05$, $Q_W = 11.12$, $p = 0.134$

Consistency in results	Consistent for all except global cognition, processing speed, problem solving, social cognition, global functioning.
Precision in results	Precise
Directness of results	Indirect comparison (mixed control conditions combined).

Explanation of acronyms

BPRS = Brief Psychiatric Rating Scale, CI = Confidence Interval, CT = cognitive training, *d* = Cohen's *d* and *g* = Hedges' *g* = standardized mean differences (see below for interpretation of effect size), MD = mean difference, N = number of participants, NS = not significant, OR = odds ratio, *p* = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), Q = Q statistic for the test of heterogeneity, Q_W = test for within group differences (heterogeneity in study results within a group of studies – measure of study consistency), Q_B = test for between group differences (heterogeneity between groups of studies for an outcome of interest), RCT = randomised controlled trial, vs = versus, WAIS = Weschler Adult Intelligence Scale, WCST = Wisconsin Card Sorting Test

Explanation of technical terms

* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias – selective reporting of results; publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small[19].

† Different effect measures are reported by different reviews.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. 0.2 represents a small effect, 0.5 a medium effect, and 0.8 and over represents a large effect[19].

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or < 0.2[20]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios

Margarete Ainsworth Building, Barker Street, Randwick NSW 2031. Phone: 02 9399 1000. Email: info@neura.edu.au

measure the effect of an explanatory variable on the hazard or risk of an event.

Correlation coefficients (eg, r) indicate the strength of association or relationship between variables. They can provide an indirect indication of prediction, but do not confirm causality due to possible and often unforseen confounding variables. An r of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised (*b*) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent considerable heterogeneity and over this is considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula;

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

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, these criteria should be relaxed[21].

‖ Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and/or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available and is therefore inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.

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