TECHNICAL COMMENTARY

Cognitive remediation

Introduction

Cognitive impairment is a significant problem for many people with schizophrenia, effecting domains such as executive functioning, attention, memory and social cognition. 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 as well as social skills and communication. 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.

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 prioritised 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[1]. 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[2] 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).

Results

We found seven systematic reviews that met our inclusion criteria[3-9].

- Moderate to high quality evidence finds a medium-sized benefit of computerised or

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non-computerised cognitive remediation over control interventions for improving attention, memory, processing speed, problem solving, cognitive flexibility and social functioning. There was also a small benefit for symptoms and for overall functioning.

- Moderate to low quality evidence finds similar effectiveness in short (<15 sessions) and long duration of cognitive remediation (>15 sessions), and that strategy learning may be more effective than rehearsal learning.
- For computerised cognitive drill and practice training, moderate to high quality evidence finds small to medium-sized improvements in attention and positive symptoms when compared to control conditions. There was also a small improvement in functioning. Moderate quality evidence finds medium-sized improvements in working memory and depressive symptoms, and small improvements in psychomotor speed. There were also small trend improvements in verbal fluency and verbal and visual learning and memory. Small trend improvements were found for negative and total symptoms with computerised cognitive drill and practice training.
- Moderate to high quality evidence finds a medium-sized benefit of improved theory of mind with observation and imitation of social emotions interventions.

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Kambeitz-Ilankovic L, Betz LT, Dominke C, Haas SS, Subramaniam K, Fisher M, Vinogradov S, Koutsouleris N, Kambeitz J

Multi-outcome meta-analysis (MOMA) of cognitive remediation in schizophrenia: Revisiting the relevance of human coaching and elucidating interplay between multiple outcomes

Neuroscience and Biobehavioral Reviews 2019; 107: 828-45

View review abstract online

Comparison	**Cognitive remediation with or without supplementary human guidance vs. an active control condition (e.g. video games).**
Summary of evidence	**Moderate to high quality evidence (large sample, consistent, precise, indirect) suggests cognitive remediation provided a small benefit over active control interventions for improving cognitive skills, negative and affective symptoms, and overall functioning. Authors report that cognitive gains trigger restoration of psychosocial functioning which in turn facilitates improvement in clinical symptoms.**

Cognition

A small, significant effect showed improved overall cognition with cognitive remediation;

70 samples, N = 4,067, g = 0.28, 95%CI 0.21 to 0.34, $p < 0.001$, I^2 = 3.5%

Significant effects were found for attention (g = 0.23), verbal memory (g = 0.21), social cognition (g = 0.18), working memory (g = 0.27), processing speed (g = 0.22), and reasoning (g = 0.25), but not for visual memory (g = 0.12).

Earlier studies publishing effects of the CR on processing speed reported larger effects. Longer duration of cognitive training was associated with a smaller effect on attention. Younger samples, samples with shorter illness duration, and samples with more females all showed better performance on reasoning and problem-solving. Similarly, the effectiveness of cognitive remediation increased global cognition in samples with shorter illness duration.

Compared to studies not using supplementary human guidance, studies using human guidance found significantly larger effects for working memory (g = 0.34 vs. 0.16), verbal memory (g = 0.30 vs. 0.09) and real-world cognitive skills (g = 0.35 vs. 0.08).

Symptoms

Small, significant effects of improved negative and depressive/anxious symptoms with cognitive remediation; Negative: 32 samples, N not reported, g = 0.13, 95%CI 0.02 to 0.25, p = 0.026, I^2 = 32% Depressive/anxious: 14 samples, N not reported, g = 0.25, 95%CI 0.09 to 0.40, p = 0.002, I^2 = 14% No significant effects were found for positive (g = 0.06), general (g = 0.05), and total symptoms (g = 0.10). There were no differences between studies using or not using supplementary human guidance.
Functioning
A small, significant effect of improved functioning with cognitive remediation; 49 samples, N not reported, g = 0.16, 95%CI 0.06 to 0.25, p = 0.001, I^2 = 34% Significant effects were found for social cognition (g = 0.26) and work outcomes (g = 0.40), but not for health (g = 0.10), quality of life (g = 0.14), or functioning global (g = 0.04). There were no differences between studies using or not using supplementary human guidance.

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

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 (large samples, consistent, precise, indirect) suggests cognitive remediation provided a medium-sized benefit over control interventions for improving 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.
Cognition	
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. *A medium-sized effect of improved cognition with cognitive remediation;* 12 trials (10 randomised), N = 543, d = 0.45, 95%CI 0.26 to 0.64, $p < 0.05$, $Q_W = 14.3$, $p = 0.43$ <u>Subgroup analysis: duration of training</u> *Medium-sized effects in both short and long duration of training;* <15 sessions (mean = 7.7 sessions): 5 studies, d = 0.44, 95%CI 0.01 to 0.85, $p < 0.05$ >15 sessions (mean = 33 sessions): 6 studies, d = 0.45, 95%CI 0.18 to 0.85, $p < 0.05$ Effect sizes were not significantly different: $Q_B = 0.001$, $p = 0.978$ <u>Subgroup analysis: type of training</u> *Medium-sized effect of improved cognition with strategy learning, but not rehearsal learning;* Strategy learning: 7 studies, d = 0.52, 95%CI 0.25 to 0.78, $p < 0.05$ Rehearsal learning: 6 studies d = 0.34, 95%CI -0.03 to 0.70, $p > 0.05$ Although effect sizes were not significantly different: $Q_B = 0.95$, $p = 0.36$	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Indirect (mixed control conditions).

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 vs. no treatment, a placebo intervention, or standard treatment for improving executive functioning.**
Summary of evidence	**Moderate quality evidence (medium-sized samples, consistent,**

	precise, indirect) suggests a large effect of improved cognitive flexibility with cognitive remediation.
Cognitive flexibility	
A large effect of improved cognitive flexibility with cognitive remediation; 11 studies, N = 181, *d* = 0.98, 95%CI 0.80 to 1.16, $p < 0.05$, $Q_W = 17.6$, $p = 0.61$ WCST: categories 9 studies, *d* = 1.08, 95%CI 0.80 to 1.37, $p < 0.05$, $Q_W = 5.80$ *p* not reported WCST: perseverative errors 8 studies, *d* = 0.93, 95%CI 0.64 to 1.21, $p < 0.05$, $Q_W = 9.10$ *p* not reported WCST: conceptual learning 4 studies, *d* = 0.90, 95%CI 0.52 to 1.28, $p < 0.05$, $Q_W = 1.95$ *p* not reported Effect sizes were not significantly different: $Q_B = 0.79$, $p = 0.68$	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Indirect (mixed control conditions are combined).

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 (computerised and non-computerised) vs. a control condition (passive or active control) for cognitive skills.**

Cognitive remediation

Summary of evidence	**Moderate to high quality evidence (large samples, consistent, precise, indirect) suggests cognitive remediation provides medium-sized benefit for improving attention, processing speed, problem solving, and social cognition, and a small benefit for symptoms. Moderate quality evidence (inconsistent) suggests cognitive remediation provides medium-sized benefit for improving verbal working memory and a small benefit for general functioning, with no benefit for visual learning and visual memory.**

Cognition

A medium-sized effect of improved global cognition with cognitive remediation;

26 RCTs, N = 1,214, *d* = 0.41, 95%CI 0.29 to 0.52, *p* < 0.001, Q_W = 35.3, *p* = NS

This effect was evident 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

A significant, medium-sized effect of improved attention/vigilance;

N = 659, *d* = 0.41, 95%CI 0.25 to 0.57, *p* < 0.001, Q_W = 9.8, *p* = NS

A significant, medium-sized effect of improved processing speed;

N = 655, *d* = 0.48, 95%CI 0.28 to 0.69, *p* < 0.001, Q_W = 20.7, *p* = NS

A significant, medium-sized effect of improved verbal working memory;

N = 428, *d* = 0.52, 95%CI 0.33 to 0.72, *p* < 0.001, Q_W = 3.9, *p* = NS

A significant, small to medium-sized effect of improved verbal learning and memory;

N = 858, *d* = 0.39, 95%CI 0.20 to 0.58, *p* < 0.001, Q_W = 26.6, *p* < 0.05

A significant, medium-sized effect of improved reasoning and problem solving;

N = 564, *d* = 0.47, 95%CI 0.30 to 0.64, *p* < 0.001, Q_W = 21.8, *p* = NS

A significant, medium-sized effect of improved social cognition;

N = 228, *d* = 0.54, 95%CI 0.22 to 0.88, *p* < 0.001, Q_W = 2.8, *p* = NS

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

Symptoms and functioning

A significant, small effect of improved symptoms;

N = 709, *d* = 0.28, 95%CI 0.13 to 0.43, *p* < 0.001, Q_W = 12.2, *p* = NS

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A significant, small to medium-sized effect of improved functioning; 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 (mixed control conditions are combined).

Prikken M, Konings MJ, Lei WU, Begemann MJH, Sommer IEC

The efficacy of computerized cognitive drill and practice training for patients with a schizophrenia-spectrum disorder: A meta-analysis

Schizophrenia Research 2019; 204: 368-74

View review abstract online

Comparison	**Computerised cognitive drill and practice training vs. a control condition (passive or active control).**
Summary of evidence	**Moderate to high quality evidence (large samples, consistent, precise, indirect) finds small to medium-sized improvements in attention and positive symptoms with computerised cognitive drill and practice training when compared to control conditions. There was a small improvement in functioning, and no improvements in general cognition compared to control conditions.** **Moderate quality evidence (inconsistent or small to medium-sized samples) also finds medium-sized improvements in depressive symptoms and working memory, and small improvements in psychomotor speed. There were small trend improvements in negative and total symptoms, in verbal fluency, and in verbal and visual learning and memory. There was no improvement in general symptoms when compared to control conditions.**
Cognition	
The following cognitive domains were improved with computerized cognitive drill and practice training (small or small to medium effects);	

Psychomotor speed: 16 studies, N = 809, *g* = 0.20, 95%CI 0.00 to 0.41, *p* = 0.05, I^2 = 53%, *p* = 0.01
Attention: 12 studies, N = 669, *g* = 0.31, 95%CI 0.13 to 0.50, *p* = 0.001, I^2 = 31%, *p* = 0.14
This effect was largest in studies of people with long illness duration.
Working memory: 18 studies, N = 876, *g* = 0.38, 95%CI 0.21 to 0.55, *p* < 0.001, I^2 = 36%, *p* = 0.07
This effect was largest in studies with a high risk of bias and was smallest in studies of people with a long illness duration.
There were trend effects of improvement in;
Verbal fluency: 6 studies, N = 272, *g* = 0.21, 95%CI -0.03 to 0.45, *p* = 0.09, I^2 = 2%, *p* = 0.40
Verbal learning & memory: 18 studies, N = 863, *g* = 0.23, 95%CI -0.01 to 0.48, *p* = 0.06, I^2 = 69%, *p* < 0.001
This effect was smallest in studies of people with a long illness duration.
Visual learning & memory: 10 studies, N = 551, *g* = 0.28, 95%CI -0.02 to 0.57, *p* = 0.06, I^2 = 67%, *p* = 0.001
This effect was smallest in studies of people with a long illness duration.
There were no significant differences between groups for;
General cognition: 9 studies, N = 467, *g* = 0.03, 95%CI -0.17 to 0.23, *p* = 0.75, I^2 = 14%, *p* = 0.32
Social cognition: 3 studies, N = 113, *g* = -0.07, 95%CI -0.47 to 0.33, *p* = 0.72, I^2 = 13%, *p* = 0.32
Reasoning & problem solving: 14 studies, N = 752, *g* = 0.16, 95%CI -0.11 to 0.43, *p* = 0.25, I^2 = 71%, *p* = 0.001
Symptoms and functioning
The following symptoms were improved with computerized cognitive drill and practice training (all small effects);
Positive symptoms: 10 studies, N = 502, *g* = 0.31, 95%CI 0.10 to 0.51, *p* = 0.003, I^2 = 24%, *p* = 0.22
This effect was largest in studies with an active control.
Depression: 5 studies, N = 273, *g* = 0.37, 95%CI 0.14 to 0.61, *p* = 0.002, I^2 = 0%, *p* = 0.51
There were trend effects of improvement in;
Functioning: 10 studies, N = 521, *g* = 0.19, 95%CI -0.01 to 0.39, *p* = 0.07, I^2 = 27%, *p* = 0.20
Negative symptoms: 11 studies, N = 536, *g* = 0.22, 95%CI -0.04 to 0.49, *p* = 0.10, I^2 = 57%, *p* = 0.01
Total symptoms: 6 studies, N = 279, *g* = 0.29, 95%CI -0.06 to 0.64, *p* = 0.10, I^2 = 52%, *p* = 0.07
There were no significant differences between groups in general symptoms;
6 studies, N = 280, *g* = 0.03, 95%CI -0.20 to 0.26, *p* = 0.78, I^2 = 0%, *p* = 0.84

Consistency in results	Consistent for attention, verbal fluency, general cognition, social

	cognition, positive symptoms, depression, functioning, and general symptoms.
Precision in results	Precise
Directness of results	Indirect (mixed control conditions are 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 vs. a control condition for global cognitive ability.**
Summary of evidence	**Moderate quality evidence (large sample, mostly inconsistent, precise, indirect) suggests a medium-sized benefit for improving global cognition, with benefits 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

A medium-sized effect for improving global cognition;

38 studies, N = 1,982, d = 0.448, 95%CI 0.306 to 0.590, $p < 0.05$, $Q_W = 76.18$, $p < 0.001$

Small to medium-sized benefits for;

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 = 1,332, 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 = 1,029, 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 = 1,346, 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 = 1,389, 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 *Small benefits for;* Symptom severity: 20 studies, N = 1,114, *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 = 1,036, *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 (mixed control conditions combined).

Yeh P-Y, Yu L, Guo N-W, Lin W-C, Wu C-K

Observation and imitation of social emotions are essential for improving cognitive and affective theory of mind in schizophrenia: A meta-analysis

Journal of Nervous and Mental Disease 2019; 207: 474-81

View review abstract online

Comparison	**Observation and imitation of social emotions with or without cognitive training vs. treatment as usual or cognitive remediation alone.**
Summary of evidence	**Moderate to high quality evidence (large sample, consistent,**

	precise, indirect) suggests a medium-sized benefit of improved theory of mind with observation and imitation of social emotions interventions.
Theory of mind	
Medium-sized effect showed theory of mind improved with observation and imitation of social emotions; All theory of mind: 14 studies, N = 494, *g* = 0.51, 95%CI 0.33 to 0.69, *p* < 0.001, I^2 = 0% Cognitive theory of mind: 13 studies, N not reported, *g* = 0.53, 95%CI 0.29 to 0.76, *p* < 0.001, I^2 = 34% Affective theory of mind: 11 studies, N not reported, *g* = 0.54, 95%CI 0.34 to 0.73, *p* < 0.001, I^2 = 0% Subgroup analysis showed the effect sizes were larger in studies without supplementary cognitive training.	
Consistency in results	Consistent
Precision in results	Precise
Directness of results	Indirect (mixed conditions).

Explanation of acronyms

CI = confidence interval, *d* = Cohen's *d* and *g* = Hedges' *g* = standardised mean differences, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), 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, WCST = Wisconsin Card Sorting Test

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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[10].

† 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[10].

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[11]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios

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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[12].

‖ 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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References

1. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMAGroup (2009): Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *British Medical Journal* 151: 264-9.
2. GRADEWorkingGroup (2004): Grading quality of evidence and strength of recommendations. *British Medical Journal* 328: 1490.
3. Krabbendam L, Aleman A (2003): Cognitive rehabilitation in schizophrenia: a quantitative analysis of controlled studies. *Psychopharmacology* 169: 376-82.
4. McGurk SR, Twamley EW, Sitzer DI, McHugo GJ, Mueser KT (2007): A meta-analysis of cognitive remediation in schizophrenia.[see comment]. *American Journal of Psychiatry* 164: 1791-802.
5. Kurtz MM, Moberg PJ, Gur RC, Gur RE (2001): Approaches to cognitive remediation of neuropsychological deficits in schizophrenia: a review and meta-analysis. *Neuropsychology Review* 11: 197-210.
6. Wykes T, Huddy V, Cellard C, McGurk SR, Czobor P (2011): A Meta-Analysis of Cognitive Remediation for Schizophrenia: Methodology and Effect Sizes. *Am J Psychiatry*: appi.ajp.2010.10060855.
7. Prikken M, Konings MJ, Lei WU, Begemann MJH, Sommer IEC (2019): The efficacy of computerized cognitive drill and practice training for patients with a schizophrenia-spectrum disorder: A meta-analysis. *Schizophrenia Research* 204: 368-74.
8. Kambeitz-Ilankovic L, Betz LT, Dominke C, Haas SS, Subramaniam K, Fisher M*, et al.* (2019): Multi-outcome meta-analysis (MOMA) of cognitive remediation in schizophrenia: Revisiting the relevance of human coaching and elucidating interplay between multiple outcomes. *Neuroscience and Biobehavioral Reviews* 107: 828-45.
9. Yeh P-Y, Yu L, Guo N-W, Lin W-C, Wu C-K (2019): Observation and imitation of social emotions are essential for improving cognitive and affective theory of mind in schizophrenia: A meta-analysis. *Journal of Nervous and Mental Disease* 207: 474-81.
10. CochraneCollaboration (2008): Cochrane Handbook for Systematic Reviews of Interventions. Accessed 24/06/2011.
11. Rosenthal JA (1996): Qualitative Descriptors of Strength of Association and Effect Size. *Journal of Social Service Research* 21: 37-59.
12. GRADEpro (2008): [Computer program]. Jan Brozek, Andrew Oxman, Holger Schünemann. *Version 32 for Windows*