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

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ABSTRACT

Background: Computerized methods for improving cognitive functioning in schizophrenia have gained popularity during the past decades. Therefore, this study evaluates the available evidence for the efficacy of computerized cognitive drill and practice training for patients with schizophrenia-spectrum disorders.
Methods: A systematic search was carried out using PubMed, Embase, Cochrane Database of Systematic Reviews, and PsycINFO. A meta-analysis was performed to compare cognitive drill and practice training in patients with a schizophrenia-spectrum disorder with non-cognitively oriented control conditions. The primary outcome was cognitive functioning. Secondary outcome measures included psychotic symptoms, depressive symptoms, and functional outcomes. Effect sizes (ES) for all included studies were calculated as Hedges' *g*.
Results: 24 studies were included with 1262 patients in total. Compared to a control condition, patients receiving computerized cognitive drill and practice training showed significantly more improvement on attention (ES = 0.31, $p = 0.001$), working memory (ES = 0.38, $p < 0.001$), positive symptoms (ES = 0.31, $p = 0.003$), and depressive symptoms (ES = 0.37, $p = 0.002$). Small, marginally significant effect sizes were found for processing speed, verbal and visual learning and memory, and verbal fluency. However, significant effects on functional outcomes and social cognition were absent.
Discussion: The current study showed evidence for the efficacy of computerized cognitive drill and practice training in patients with schizophrenia-spectrum disorders. However, the absence of effects on social cognition and functional outcomes questions the generalization of treatment effects. Together, these results stimulate further development of computerized training programs for schizophrenia that not only improve cognitive functioning, but also generalize cognitive improvement to functional outcomes.

1. Introduction

During the past decades, an increasing amount of computerized programs have been developed to enhance cognitive performance, such as Nintendo's 'Brain age' or PositScience's 'BrainHQ'. These programs use a principle of repeated practice of tasks (i.e., drill and practice training) to improve cognitive functioning. Interestingly, this principle has also been adopted in the design of computerized cognitive rehabilitation programs for patients with schizophrenia-spectrum disorders (e.g., CogPack and CogRehab). These computer programs have numerous advantages, such as the possibility to automatically adjust practice levels, standardization of instructions, and the possibility to perform the training with only little help from therapist, thereby reducing costs (Burda et al., 1994). However, evidence for the efficacy of such programs in improving (cognitive) functioning remains unclear.

In general, cognitive functioning in patients with schizophrenia-spectrum disorders is between one and two standard deviations below normal and includes dysfunction in the domains of attention/vigilance, reasoning and problem solving, working memory, processing speed, verbal learning and memory, visual learning and memory, and social cognition (Kern et al., 2011; Nuechterlein et al., 2004). Antipsychotic treatment, the main pharmacological treatment for schizophrenia, has a minimal effect on these symptoms (Hill et al., 2010; Nielsen et al., 2015). As cognitive deficits are related to decreased daily functioning and work performance, improvement of cognitive functioning is extremely important for patients´ quality of life (Bowie and Harvey, 2006; Green et al., 2000; McGurk et al., 2007). When developing treatment programs for schizophrenia, the presence of amotivation has to be taken into account, as this is one of the symptoms of the disorder (American Psychiatric Association, 2013). The use of gaming elements in computerized cognitive training might help overcome this problem,

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as it can make a treatment program increasingly meaningful, appealing, motivating, and feasible (Fleming et al., 2017; Lau et al., 2017; Medalia et al., 2001; Stapleton and Taylor, 2003).

Various studies have investigated the efficacy of drill and practice exercises in the treatment of cognitive deficits in schizophrenia to evaluate whether such programs have potential for this patient population, with inconsistent findings. Importantly, drill and practice training differs from strategic training, in which the goal is to improve performance by explicitly learning and applying cognitive strategies, such as mnemonics (Wykes et al., 2011). Previous meta-analyses showed that cognitive training can improve cognitive functioning in patients with schizophrenia-spectrum disorders, but they did not include computerized training specifically (McGurk et al., 2007; Wykes et al., 2011). In 2011 a meta-analysis was published that *did* focus on computerized training only and also showed positive results (Grynszpan et al., 2011). To our knowledge, the previous meta-analyses included both drill and practice and strategic training and coaching (Grynszpan et al., 2011; McGurk et al., 2007; Wykes et al., 2011). Importantly, as computerized training programs and games gain popularity, we aim to assess the efficacy of computerized drill and practice cognitive remediation on neurocognitive functioning in schizophrenia. Furthermore, we aim to assess generalization of cognitive improvement to other domains: social cognition, psychotic and depressive symptoms, and functional outcomes.

2. Methods

2.1. Literature search

This meta-analysis was conducted following the Preferred Reporting for Systematic Reviews and Meta-analysis (PRISMA) Statement (Moher et al., 2010). Four databases were systematically searched: PubMed (MEDLINE), Embase, Cochrane Database of Systematic Reviews, and PsycINFO, by two independent researchers (W.L. and M.K.). A combination of the following search terms was used: "cognitive," "cognition," "neuropsychological," "game," "computer," "computerized," "training," "remediation," "rehabilitation," "enhancement," "schizophrenia," "schizoaffective," "schizophreniform," and "psychosis" (see Supplement 1 for search strings). Studies were included after consensus between M.P., W.L., and M.K. The cut-off date for the search was November 23, 2017. Cross-referencing was performed for all the papers included in the final meta-analyses. The search did not impose year or language restrictions. Authors were contacted if necessary in order to obtain study details.

2.2. In- and exclusion criteria

Selected articles met the following criteria:

- trials that assessed the effect of any computerized cognitive drill and practice training, as compared to an active or passive control condition. Passive control conditions included placebo, no treatment, standard care, a waiting list control group, watching TV, or self-chosen internet use, whereas active control conditions included interventions with the same intensity or duration as the experimental condition (e.g., occupational treatment (Bosia et al., 2007) or performing a computerized typing program (Gomar et al., 2015))
- included patients had a diagnosis of schizophrenia or schizophrenia spectrum disorder (schizoaffective disorder, schizophreniform disorder, delusional disorder, persistent delusional disorder, or psychosis not otherwise specified according to the diagnostic criteria of the Diagnostic and Statistical Manual of mental Disorders (DSM-III, DSM-III-R, DSM-IV, DSM-IV-TR, DSM-5) or the International Classification of Diseases-9 or −10)
- outcome measures covered at least one of the following domains: cognition, psychotic symptoms, depressive symptoms or functional outcomes (see paragraph 'outcome measures')
- the study reported means and SD's, *F*-values, or *p*-values, so that the effect size could be calculated, or data were provided by the author after they were contacted

Articles were excluded when:

- the control group used computer games that highly rely on cognitive functioning (e.g. Sudoku, crossword puzzles). More specifically, as the effect of *cognitive training* is assessed in this meta-analysis, cognition should only be targeted in the computerized cognitive training group and not in the control condition
- additional to the cognitive treatment, another treatment is given (such as group therapy) which was not accounted for in the control group. Thus, the specific effect of the cognitive treatment must be traceable
- cognitive strategies were taught in the cognitive training intervention
- healthy individuals were used as a control group
- only baseline data was provided

2.3. Outcome measures

Primary outcome measures included eight cognitive domains plus general cognitive functioning. The latter could either be measured by cognitive test batteries or calculated by the authors as the mean of all included cognitive tests in that specific study. The cognitive domains were based on the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) guidelines (Nuechterlein et al., 2004): 1. attention/vigilance, 2. reasoning and problem solving, 3. working memory, 4. processing speed, 5. verbal learning and memory, 6. visual learning and memory, and 7. social cognition. Furthermore, the retrieved data permitted us to divide the processing speed domain into psychomotor speed and verbal fluency. Secondary outcome measures were psychotic symptoms, depressive symptoms, and functional outcome (i.e., assessment of global, social or vocational functioning). Supplement 2 provides an overview of all tests that were included for each outcome measure.

2.4. Outcome selection

When a study used more than one cognitive test was used to evaluate one cognitive domain, we chose the test that was used most often in the included studies. Furthermore, if multiple subtask or scores of a test were reported, we used the subtask or score that best represented the cognitive domain, based on information from test manuals Also, because the use of an active control group accounts for potential therapeutic effects (Karlsson and Bergmark, 2015), an active control group was preferred over a passive one when both were included in one study. One study reported results for completers and non-completers separately; completer data were used (Byrne et al., 2013).

2.5. Statistical analyses

Statistical information was independently extracted from the included studies by two researchers (M.K. and W.L.) and was then compared until consensus was reached (between M.P., M.K., and W.L.). Comprehensive Meta-analysis software version 2.0 was used to perform all analyses (Bax et al., 2007). Hedges' g was calculated to quantify effect sizes and studies were combined using a random effects model. A random effects model was chosen because of the variable population parameters in the included studies (Field and Gillett, 2010). Effect sizes were categorized as small (>0.20), medium (>0.50), or large (>0.80) (Maher et al., 2013). The use of mean change scores and corresponding *SD*'s per treatment arm was preferred over separate pre- and post-means and corresponding *SD*'s per treatment arm. *F*- or *t*-values and

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corresponding p-values were used when mean change or means were not available. A p-value of <0.05 was considered as significant.

The Q-value and I^2-statistic were evaluated in order to examine whether studies could be combined to share a common population effect size. The Q-value tests heterogeneity, using a chi-square distribution with k-1 degrees of freedom (k = number of studies). A Q-value higher than the degrees of freedom indicates significant between-study variability (i.e., heterogeneity). I^2 shows the percentage of total variation amongst the included studies that is due to differences in true effect size rather than a sampling error. I^2 of 25%, 50%, and 75% can be interpreted as low, moderate, and high heterogeneity (Higgins et al., 2003).

To assess the possibility of publication bias, funnel plots were visually checked for (a)symmetry (Egger et al., 1997). Additionally, Egger's test was used to quantify bias captured by the funnel plot, where a significant effect indicates evidence for publication bias. Furthermore, the fail-safe number (N_R) was calculated to demonstrate how many studies would be needed to turn a significant effect into a non-significant effect (Rosenthal, 1979). N_R should be at least five times the number of studies included in the meta-analysis +10 to rule out the file-drawer problem (Rosenthal, 1979). The analyses described above were repeated without the only non-randomized study that was included (Trapp et al., 2013).

Meta-regression was performed for the variables age, illness duration, treatment duration, and methodological bias. An overview of methodological bias in the included studies is provided in Supplement 3. This assessment was done by using the Cochrane risk of bias criteria: selection bias, performance bias, detection bias, attrition bias, and reporting bias (Higgins and Green, 2011). An overview of these criteria in the included studies can be found in Supplement 3. Also, subgroup analyses were performed to compare two types of control condition: active and passive.

3. Results

Fig. 1 shows the PRISMA flow diagram (Moher et al., 2010). The search resulted in a total of 24 studies including 1262 patients suitable for the quantitative synthesis of this meta-analysis (Bellucci et al., 2002; Benedict et al., 1994; Bosia et al., 2007; Burda et al., 1994; Byrne et al., 2013; Cavallo et al., 2013; D'Amato et al., 2011; D'Souza et al., 2013; Gomar et al., 2015; Horan et al., 2011; Hubacher et al., 2013; Kurtz et al., 2007; Lee, 2013; Liao et al., 2016; Linke et al., 2017; Lopez-Martin et al., 2017; Mak et al., 2013; Man et al., 2012; Medalia et al., 1998; Pitschel-Walz et al., 2013; Rass et al., 2012; Sartory et al., 2005; Trapp et al., 2013; Vita et al., 2011). Details of these included studies can be found in Supplement 4. Meta-analytic results regarding all outcome measures are reported in Table 1 and corresponding forest plots can be found in Supplement 5. There were no outliers (SE ± 2.96) in any of the analyses.

3.1. Primary outcome measures: cognition

Patients receiving computerized cognitive training showed significantly more improvement than a control condition on the domains of attention (Hedges' $g = 0.31$) and working memory (Hedges' $g = 0.38$; Table 1 and Fig. 2). Heterogeneity was low for these domains. Eggers test was non-significant in all analyses, indicating absence of publication bias. N_R was low for attention, which means that the file-drawer problem could not be ruled out for the analysis of this domain. Small to moderate effect sizes were also found for processing speed, visual learning and memory, verbal learning and memory, and verbal fluency, which were marginally significant. There was no significant effect on general cognition, reasoning and problem solving, and social cognition. Conclusions remained the same when the only non-randomized study was excluded from the analyses (Trapp et al., 2013).

3.2. Secondary outcome measures: psychotic symptoms, depressive symptoms and functional outcomes

Positive (Hedges' $g = 0.31$) and depressive symptoms (Hedges' $g = 0.37$) improved significantly after computerized cognitive training relative to a control condition (Table 1 and Fig. 3). Heterogeneity was low in these analyses, but a low N_R indicated that the file-drawer problem could not be ruled out. Small to moderate, but only marginally significant effects on negative symptoms, total symptoms, and functional outcomes were found. There was no effect of cognitive training on general symptoms. Conclusions remained the same when the only non-randomized study was excluded from the analyses (Trapp et al., 2013).

3.3. Moderator analysis

Meta-regression showed no influence of age on the efficacy of computerized cognitive training. However, a significant positive association between illness duration and effect sizes was found for the attention domain ($B = 0.05$, S.E. $= 0.02$, $z = 2.55$, $p = 0.01$, $k = 7$). Also, longer treatment duration was negatively related to effect sizes in the domains of working memory ($B = -0.01$, S.E. $= 0.005$, $z = -2.43$, $p = 0.02$, $k = 17$), verbal learning and memory ($B = -0.02$, S.E. $= 0.01$, $z = -2.31$, $p = 0.02$, $k = 17$), and visual learning and memory ($B = -0.02$, S.E. $= 0.01$, $z = -2.20$, $p = 0.03$, $k = 9$). Furthermore, a positive relation was found between effect sizes in the working memory domain and risk of bias score ($B = 0.92$, S.E. $= 0.46$, $z = -2.01$, $p = 0.04$, $k = 18$). Last, studies that used active control conditions yielded larger effect sizes on positive symptoms compared with studies that used passive control conditions. (Q-value $= 0.65$, $p = 0.01$).

4. Discussion

Within the context of the increasing popularity of training programs that aim to improve cognitive functioning, this meta-analysis examined the efficacy of computerized cognitive drill and practice training, compared to a non-cognitively oriented control condition in patients with schizophrenia-spectrum disorders. Previous meta-analyses addressed the question whether cognitive remediation in general was effective, thereby including both computerized and paper and pencil programs, and drill and practice and strategic training (Grynszpan et al., 2011; McGurk et al., 2007; Wykes et al., 2011). Focusing on computerized drill and practice programs, 24 studies (with a total of 1262 patients) could be included and results showed that computerized cognitive training had a superior effect on attention and working memory, as well as on positive and depressive symptoms. Furthermore, small to moderate, but only marginally significant effects were found for processing speed, verbal fluency, and verbal and visual learning and memory. Results showed no convincing evidence for improvement in general cognition, reasoning and problem solving, social cognition, and functional outcomes.

These significant effects of computerized cognitive drill and practice training on attention and working memory and a trend towards a significant effect for the domains of processing speed, verbal fluency, and verbal and visual learning and memory are in line with previous meta-analyses on the effects of cognitive remediation in a broader sense (Grynszpan et al., 2011; McGurk et al., 2007; Wykes et al., 2011). More specifically, a previous meta-analysis on cognitive remediation in general showed that both drill and practice and strategic training improved cognitive outcomes (Wykes et al., 2011). However, others found a larger effect on verbal learning and memory for drill and practice training alone, rather than combined with strategic training (McGurk et al., 2007). Notably, our results for the above cognitive domains are similar to results from a previous meta-analysis on computerized training, which did not only include drill and practice, but also strategy training (Grynszpan et al., 2011). Here, we show that computerized cognitive training is also effective using only drill and practice methods.

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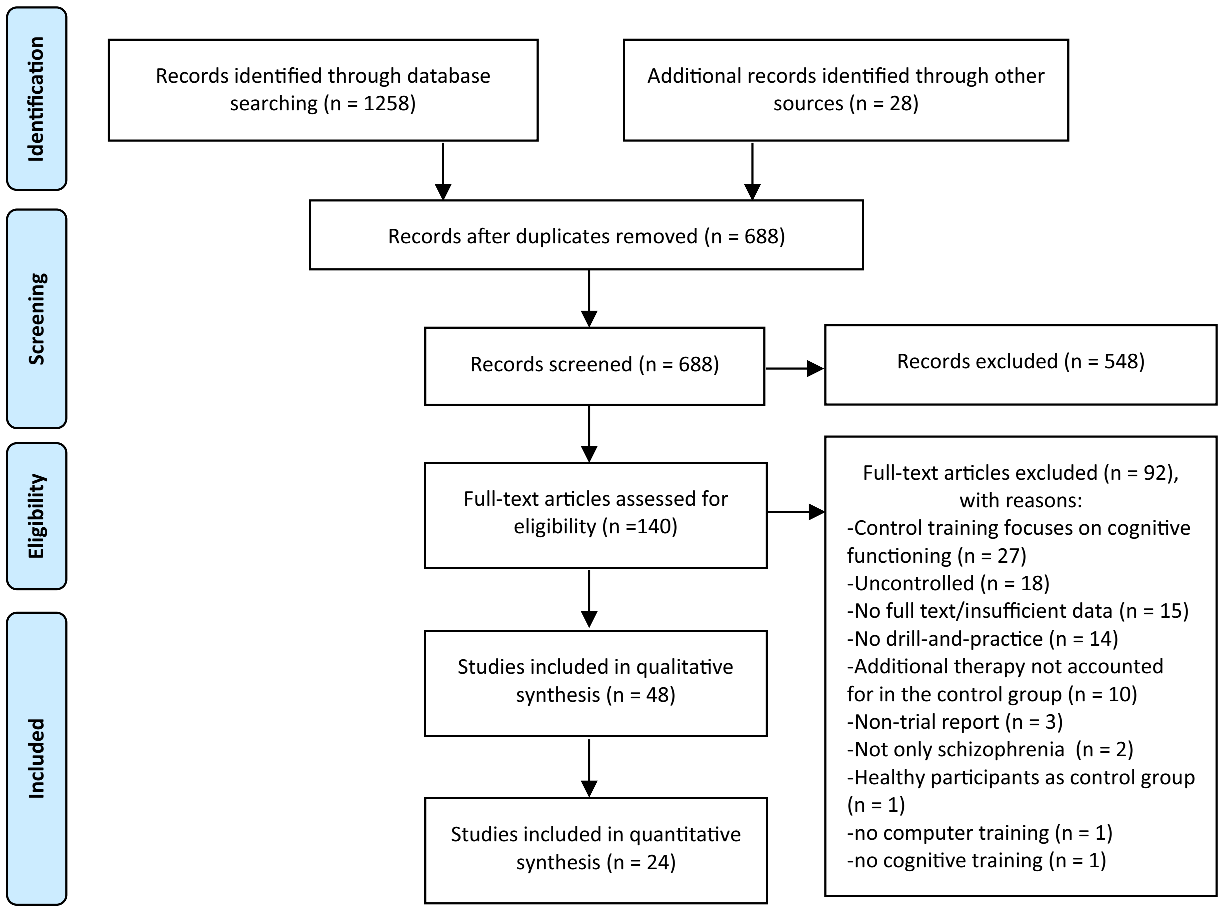

Fig. 1. PRISMA flow diagram.

No effect was found in the domain of reasoning and problem solving when comparing computerized cognitive training to a control group. This might not be surprising, as problem solving is a complex skill which is of great importance in everyday functioning (Jonassen, 2000). The absence of this effect might suggest that teaching strategies is a prerequisite for improvements in this domain. The same applies to social cognition; we found no significant effect for this domain, whereas meta-analyses that included strategy training did find such an effect (Grynszpan et al., 2011; McGurk et al., 2007; Wykes et al., 2011).

When interpreting the effects of training on cognitive functioning, some significant moderators should be taken into account. First, we found that longer illness duration was related to larger effect sizes for

Table 1
Meta-analytic results for all outcome measures.

Outcome	Nr. of studies	Nr. of patients	Effect size		Heterogeneity		Egger's test	N_R
			Hedges's *g* (95% CI)	*p*-Value	Q-value	I^2		
Primary outcomes								
General cognition	9	467	0.03 (−0.17–0.23)	0.75	Q (8) = 9.32, *p* = 0.32	14.16	*p* = 0.37	0
Attention	12	669	0.31 (0.13–0.50)	0.001[a]	Q (11) = 15.95, *p* = 0.14	31.02	*p* = 0.84	40
Reasoning & problem solving	14	752	0.16 (−0.11–0.43)	0.25	Q (13) = 45.26, *p* < 0.001	71.28	*p* = 0.41	1
Working memory	18	876	0.38 (0.21–0.55)	<0.001[a]	Q (17) = 26.50, *p* = 0.07	35.84	*p* = 0.15	130
Processing speed								
Psychomotor speed	16	809	0.20 (0.00–0.41)	0.05	Q (15) = 31.00, *p* = 0.01	53.13	*p* = 0.87	19
Verbal fluency	6	272	0.21 (−0.03–0.45)	0.09	Q (5) = 5.11, *p* = 0.40	2.23	*p* = 0.23	1
Verbal learning & memory	18	863	0.23 (−0.01–0.48)	0.06	Q (17) = 54.91, *p* < 0.001	69.04	*p* = 0.43	35
Visual learning & memory	10	551	0.28 (−0.02–0.57)	0.06	Q (9) = 27.41, *p* = 0.001	66.74	*p* = 0.64	17
Social cognition	3	113	−0.07 (−0.47–0.33)	0.72	Q (2) = 2.29, *p* = 0.32	12.79	*p* = 0.31	0
Secondary outcomes								
Positive symptoms	10	502	0.31 (0.10–0.51)	0.003[a]	Q (9) = 11.82, *p* = 0.22	23.86	*p* = 0.97	19
Negative symptoms	11	536	0.22 (−0.04–0.49)	0.10	Q (10) = 23.25, *p* = 0.01	56.99	*p* = 0.60	7
General symptoms	6	280	0.03 (−0.20–0.26)	0.78	Q (5) = 2.04, *p* = 0.84	0.00	*p* = 0.90	0
Total symptoms	6	279	0.29 (−0.06–0.64)	0.10	Q (5) = 10.34, *p* = 0.07	51.65	*p* = 0.59	3
Depressive symptoms	5	273	0.37 (0.14–0.61)	0.002[a]	Q (4) = 3.29, *p* = 0.51	0.00	*p* = 0.20	9
Functional outcome	10	521	0.19 (−0.01–0.39)	0.07	Q (9) = 12.27, *p* = 0.20	26.63	*p* = 0.28	4

[a] Significant effect sizes ($p < 0.05$).

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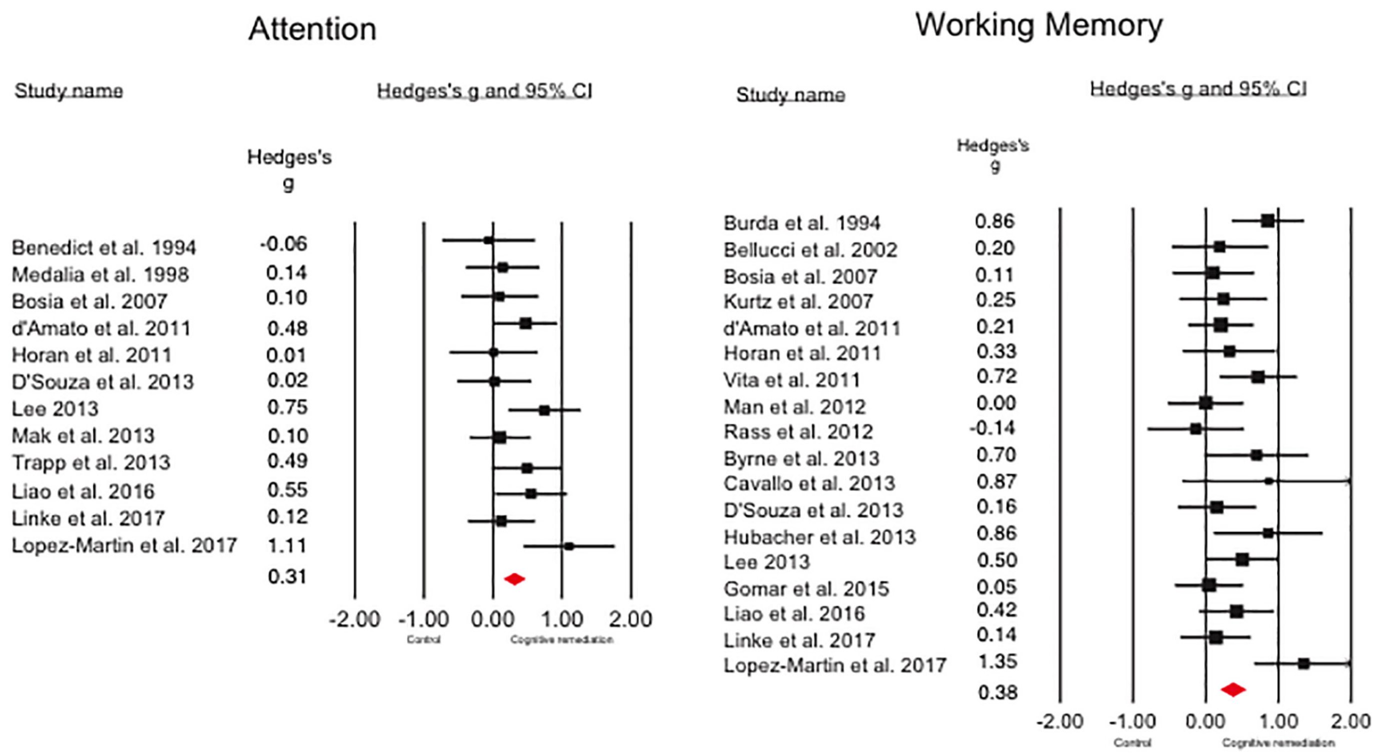

Fig. 2. Meta-analyses of the effect of computerized cognitive training on the cognitive domains that yielded significant effect sizes.

attention, implicating that patients with chronic schizophrenia should not be denied computerized cognitive training. Second, contrary to our expectations, we found that shorter treatment duration was related to higher effect sizes on working memory and visual and verbal learning and memory. A closer look at the studies with a short treatment duration revealed that some of these also applied a high frequency of training per week. For example, Sartory and colleagues trained patients for three weeks at an intensity of five times 45 min per week and Hubacher and colleagues applied an intensity of four times 45 min per week for four weeks in total (Hubacher et al., 2013; Sartory et al., 2005). Thus, this high intensity might explain the high effect sizes in these studies. Also, our finding that the presence of methodological bias was related to an increased effect size in the working memory domain suggest that studies with more methodological bias can yield more positive effects. Although this was only found in one cognitive domain, it stresses the importance of performing high-quality trials in order to prevent biased results. Last, our finding that studies with active control conditions yield larger effect sizes on positive symptoms is in contrast with

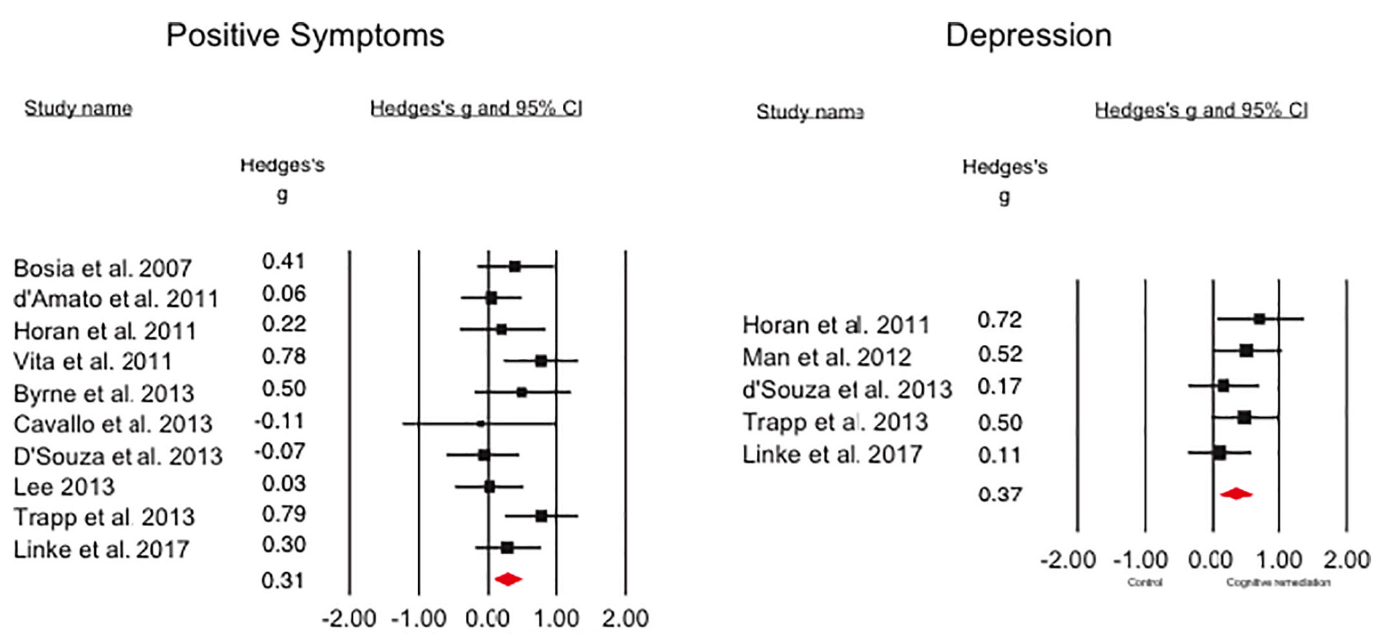

Fig. 3. Meta-analyses of the effect of computerized cognitive training on the symptoms that yielded significant effect sizes.

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previous meta-analyses, which did not find such differences (McGurk et al., 2007; Wykes et al., 2011). The fact that this analysis included only five studies per group might explain this differential finding.

Some limitations of this meta-analysis should be considered. First, computerized drill and practice methods have the potential to be performed independently by the patient. Therefore, it would be of interest to assess the effect of the amount of therapist involvement on training efficacy. Unfortunately, many included papers in the current meta-analysis did not provide sufficient information on this topic and therefore we were unable to perform such an analysis. Second, it was not possible to include all outcomes that were reported by the studies in this meta-analysis. That is, combining effect sizes of multiple tests or subscales requires knowledge of correlation coefficients between these scores. As this information was not available, we need to make a selection of the reported values. To increase comparability between studies, we selected the test/subscale that was used most often. Last, results on social cognition should be interpreted with caution, as only three papers could be included in this domain.

The current meta-analysis was the first to examine the specific effect of computerized cognitive drill and practice training on psychotic and depressive symptoms and functional outcomes. By excluding papers that employed a control condition that also targeted cognitive functioning, specific conclusions could be drawn about the efficacy of computerized drill and practice training. For more comprehensive overviews, see Wykes et al. (2011) and McGurk et al. (2007).We found significant improvement of positive and depressive symptoms after cognitive training, similar to findings regarding the effect of cognitive remediation therapy in general (Wykes et al., 2011), suggesting that computerized training programs that have the potential to be performed independently by patients, are effective. Furthermore, the analysis regarding functional outcome resulted in a very small effect, which was only marginally significant. This finding is in contrast with other meta-analyses that showed larger and significant effects (Chan et al., 2015; McGurk et al., 2007; Wykes et al., 2011). However, as these studies also included strategy training, it suggests that learning strategies might be a prerequisite for generalization of treatment effects. This might suggest that computerized cognitive training alone might not be sufficient to improve daily functioning. Importantly, our findings are in line with the main criticism on computer programs that aim to improve cognitive functioning, which is that they might not succeed in improving global cognition, and therefore have a limited effect on daily functioning (Boot and Kramer, 2014; Owen et al., 2010; Simons et al., 2016).

Taken together, although the effects of computerized cognitive drill and practice training might be small and even absent for social cognitive and functional outcome measures, it might also have benefits for patients. In fact, we found significant effects on both working memory and attention, as well as on positive and depressive symptoms. Furthermore, patients generally enjoy the computerized training programs and improvement on trained tasks can increase self-esteem and intrinsic motivation, which has beneficial effects for general treatment (Bender et al., 2004; Medalia and Revheim, 1999; Pilarc, 2000; Wykes et al., 2003). In conclusion, in clinical settings it is recommendable to discuss the possibility of adding computerized drill and practice training to standard treatment, as it might be effective in improving some cognitive functions and symptoms.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.schres.2018.07.034.

Conflict of interest

None.

Contributors

MP, ML, and WUL performed the literature search. MP and WUL created the figures. MP, MK, and WUL performed data analyses and all authors aided in data interpretation. MP and MK wrote the first draft of the paper. All co-authors read and commented on the manuscript before submission.

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References

American Psychiatric Association, 2013. Diagnostic and statistical manual of mental disorders. American Journal of Psychiatry, 5th ed. American Psychiatric Assosication, Washington, DC.

Bax, L., Yu, L.M., Ikeda, N., Moons, K.G., 2007. A systematic comparison of software dedicated to meta-analysis of causal studies. BMC Med. Res. Methodol. 7, 40.

Bellucci, D.M., Glaberman, K., Haslam, N., 2002. Computer-assisted cognitive rehabilitation reduces negative symptoms in the severely mentally ill. Schizophr. Res. 59, 225–232.

Bender, S., Dittmann-Balcar, A., Prehn, G., Thienel, R., Peters, S., Gastpar, M., 2004. How do patients with schizophrenia experience computer-based cognitive training? Nervenarzt 75, 44–50.

Benedict, R.H., Harris, A.E., Markow, T., McCormick, J.A., Nuechterlein, K.H., Asarnow, R.F., 1994. Effects of attention training on information processing in schizophrenia. Schizophr. Bull. 20, 537–546.

Boot, W.R., Kramer, A.F., 2014. The brain-games conundrum: does cognitive training really sharpen the mind? Cerebrum 15.

Bosia, M., Bechi, M., Marino, E., Anselmetti, S., Poletti, S., Cocchi, F., Smeraldi, E., Cavallaro, R., 2007. Influence of catechol-O-methyltransferase Val158Met polymorphism on neuropsychological and functional outcomes of classical rehabilitation and cognitive remediation in schizophrenia. Neurosci. Lett. 417, 271–274.

Bowie, C.R., Harvey, P.D., 2006. Cognitive deficits and functional outcome in schizophrenia. Neuropsychiatr. Dis. Treat. 2, 531–536.

Burda, P.C., Starkey, T.W., Dominguez, F., Vera, V., 1994. Computer-assisted cognitive rehabilitation of chronic psychiatric inpatients. Comput. Hum. Behav. 10, 359–368.

Byrne, L.K., Peng, D., McCabe, M., Mellor, D., Zhang, J., Zhang, T., Huang, J., Xu, Y., 2013. Does practice make perfect? Results from a Chinese feasibility study of cognitive remediation in schizophrenia. Neuropsychol. Rehabil. 23, 580–596.

Cavallo, M., Trivelli, F., Adenzato, M., Bidoia, E., Giaretto, R.M., Oliva, F., Ostacoli, L., Sala, A., Picci, R.L., 2013. Do neuropsychological and social cognition abilities in schizophrenia change after intensive cognitive training? A pilot study. Clin. Neuropsychiatry 10, 202–211.

Chan, Y.C.C., Hirai, H.W., Tsoi, K.K.F., 2015. Can computer-assisted cognitive remediation improve employment and productivity outcomes of patients with severe mental illness? A meta-analysis of prospective controlled trials. J. Psychiatr. Res. 68, 293–300.

D'Amato, T., Bation, R., Cochet, A., Jalenques, I., Galland, F., Giraud-Baro, E., Pacaud-Troncin, M., Augier-Astolfi, F., Llorca, P.M., Saoud, M., Brunelin, J., 2011. A randomized, controlled trial of computer-assisted cognitive remediation for schizophrenia. Schizophr. Res. 125, 284–290.

D'Souza, D.C., Radhakrishnan, R., Perry, E., Bhakta, S., Singh, N.M., Yadav, R., Abi-Saab, D., Pittman, B., Chaturvedi, S.K., Sharma, M.P., Bell, M., Andrade, C., 2013. Feasibility, safety, and efficacy of the combination of D-serine and computerized cognitive retraining in schizophrenia: an international collaborative pilot study. Neuropsychopharmacology 38, 492–503.

Egger, M., Smith, G.D., Schneider, M., Minder, C., 1997. Bias in meta-analysis detected by a simple, graphical test. BMJ 315, 629–634.

Field, A.P., Gillett, R., 2010. How to do a meta-analysis. Br. J. Math. Stat. Psychol. 63, 665–694.

Fleming, T.M., Bavin, L., Stasiak, K., Hermansson-Webb, E., Merry, S.N., Cheek, C., Lucassen, M., Lau, H.M., Pollmuller, B., Hetrick, S., 2017. Serious games and gamification for mental health: current status and promising directions. Front. Psychiatry 7, 215.

Gomar, J.J., Valls, E., Radua, J., Mareca, C., Tristany, J., Del Olmo, F., Rebolleda-Gil, C., Jañez-Álvarez, M., De Álvaro, F.J., Ovejero, M.R., Llorente, A., Teixidó, C., Donaire, A.M., García-Laredo, E., Lazcanoiturburu, A., Granell, L., Mozo, C.D.P., Perez-Hernández, M., Moreno-Alcázar, A., Pomarol-Clotet, E., McKenna, P.J., 2015. A multisite, randomized controlled clinical trial of computerized cognitive remediation therapy for schizophrenia. Schizophr. Bull. 41, 1387–1396.

Green, M.F., Kern, R.S., Braff, D.L., Mintz, J., 2000. Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the "right stuff"? Schizophr. Bull. 26, 119–136.

Grynszpan, O., Perbal, S., Pelissolo, A., Fossati, P., Jouvent, R., Dubal, S., Perez-Diaz, F., 2011. Efficacy and specificity of computer-assisted cognitive remediation in schizophrenia: a meta-analytical study. Psychol. Med. 41, 163–173.

Higgins, J.P.T., Green, S. (Eds.), 2011. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration. Available from www.handbook.cochrane.org.

Higgins, J.P.T., Thompson, S.G., Deeks, J.J., Altman, D.G., 2003. Measuring inconsistency in meta-analyses. BMJ [Br. Med. J.] 327, 557–560.

Hill, S.K., Bishop, J.R., Palumbo, D., Sweeney, J.A., 2010. Effect of second-generation antipsychotics on cognition: current issues and future challenges. Expert. Rev. Neurother. 10, 43–57.

Horan, W.P., Kern, R.S., Tripp, C., Hellemann, G., Wynn, J.K., Bell, M., Marder, S.R., Green, M.F., 2011. Efficacy and specificity of social cognitive skills training for outpatients with psychotic disorders. J. Psychiatr. Res. 45, 1113–1122.

Hubacher, M., Weiland, M., Calabrese, P., Stoppe, G., Stöcklin, M., Fischer-Barnicol, D., Opwis, K., Penner, I.-K., 2013. Working memory training in patients with chronic schizophrenia: a pilot study. Psychiatry J. 2013, 154867.

Jonassen, D.H., 2000. Toward a design theory of problem solving. Educ. Technol. Res. Dev. 48, 63–85.

Karlsson, P., Bergmark, A., 2015. Compared with what? An analysis of control-group types in Cochrane and Campbell reviews of psychosocial treatment efficacy with substance use disorders. Addiction 110, 420–428.

Kern, R.S., Gold, J.M., Dickinson, D., Green, M.F., Nuechterlein, K.H., Baade, L.E., Keefe, R.S.E., Mesholam-Gately, R.I., Seidman, L.J., Lee, C., Sugar, C.A., Marder, S.R., 2011. The MCCB impairment profile for schizophrenia outpatients: results from the MATRICS psychometric and standardization study. Schizophr. Res. 126, 124–131.

Kurtz, M.M., Seltzer, J.C., Shagan, D.S., Thime, W.R., Wexler, B.E., 2007. Computer-assisted cognitive remediation in schizophrenia: what is the active ingredient? Schizophr. Res. 89, 251–260.

Lau, H.M., Smit, J.H., Fleming, T.M., Riper, H., 2017. Serious games for mental health: are they accessible, feasible, and effective? A systematic review and meta-analysis. Front. Psychiatry 7, 209.

Lee, W.K., 2013. Effectiveness of computerized cognitive rehabilitation training on symptomatological, neuropsychological and work function in patients with schizophrenia. Asia Pac. Psychiatry 5, 90–100.

Liao, L., Ding, Y., Wu, X., Zhou, Y., Pan, G., 2016. A randomized controlled trial of the computerized cognitive remediation therapy to adult schizophrenia. Chin. J. Clin. Psychol. 5, 954–957.

Linke, M., Jankowski, K.S., Wichniak, A., Jarema, M., Wykes, T., 2017. Effects of cognitive remediation therapy versus other interventions on cognitive functioning in schizophrenia inpatients. Neuropsychol. Rehabil. 1–12.

Lopez-Martin, O., Segura Fragoo, A., Polonio-Lopez, M., 2017. Eficacia de un videojuego en el tratamiento de pacientes con esquizofrenia. Rev. Mex. Psycologia 34, 55–64.

Maher, J.M., Markey, J.C., Ebert-May, D., 2013. The other half of the story: effect size analysis in quantitative research. CBE Life Sci. Educ. 12, 345–351.

Mak, M., Samochowiec, J., Tybura, P., Bienkowski, P., Karakiewicz, B., Zaremba-Pechmann, L., Mroczek, B., 2013. The efficacy of cognitive rehabilitation with RehaCom programme in schizophrenia. Ann. Agric. Environ. Med. 20, 77–81.

Man, D.W.K., Law, K.M., Chung, R.C.K., 2012. Cognitive training for Hong Kong Chinese with schizophrenia in vocational rehabilitation. Hong Kong Med. J. 18, S18–S22.

McGurk, S.R., Twamley, E.W., Sitzer, D.I., McHugo, G.J., Mueser, K.T., 2007. A meta-analysis of cognitive remediation in schizophrenia. Am. J. Psychiatry 164, 1791–1802.

Medalia, A., Revheim, N., 1999. Computer assisted learning in psychiatric rehabilitation. Psychiatr. Rehabil. Skills 3, 77–98.

Medalia, A., Aluma, M., Tryon, W., Merriam, A., 1998. Effectiveness of attention training in schizophrenia. Schizophr. Bull. 24, 147–152.

Medalia, A., Revheim, N., Casey, M., 2001. The remediation of problem-solving skills in schizophrenia. Schizophr. Bull. 27, 259–267.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., 2010. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int. J. Surg. 8, 336–341.

Nielsen, R.E., Levander, S., Kjaersdam Telléus, G., Jensen, S.O.W., Østergaard Christensen, T., Leucht, S., 2015. Second-generation antipsychotic effect on cognition in patients with schizophrenia—a meta-analysis of randomized clinical trials. Acta Psychiatr. Scand. 131, 185–196.

Nuechterlein, K.H., Barch, D.M., Gold, J.M., Goldberg, T.E., Green, M.F., Heaton, R.K., 2004. Identification of separable cognitive factors in schizophrenia. Schizophr. Res. 72, 29–39.

Owen, A.M., Hampshire, A., Grahn, J.A., Stenton, R., Dajani, S., Burns, A.S., Howard, R.J., Ballard, C.G., 2010. Putting brain training to the test. Nature 465, 775–778.

Pilarc, M.J., 2000. Use of PSS CogRehab to treat psychiatric inpatients diagnosed with chronic schizophrenia. J. Cogn. Rehabil. 18, 8–10.

Pitschel-Walz, G., Gsottschneider, A., Frobose, T., Kraemer, S., Bauml, J., Jahn, T., 2013. Neuropsychology of psychoeducation in schizophrenia: results of the Munich COGPIP study. Nervenarzt 84, 79–90.

Rass, O., Forsyth, J.K., Bolbecker, A.R., Hetrick, W.P., Breier, A., Lysaker, P.H., O'Donnell, B.F., 2012. Computer-assisted cognitive remediation for schizophrenia: a randomized single-blind pilot study. Schizophr. Res. 139, 92–98.

Rosenthal, R., 1979. The file drawer problem and tolerance for null results. Psychol. Bull. 86, 638–641.

Sartory, G., Zorn, C., Groetzinger, G., Windgassen, K., 2005. Computerized cognitive remediation improves verbal learning and processing speed in schizophrenia. Schizophr. Res. 75, 219–223.

Simons, D.J., Boot, W.R., Charness, N., Gathercole, S.E., Chabris, C.F., Hambrick, D.Z., Stine-Morrow, E.A.L., 2016. Do "brain-training" programs work? Psychol. Sci. Public Interest 17, 103–186.

Stapleton, A., Taylor, P., 2003. Why videogames are cool and school sucks! Proceedings of the Annual Australian Game Developers Conference.

Trapp, W., Landgrebe, M., Hoesl, K., Lautenbacher, S., Gallhofer, B., Gunther, W., Hajak, G., Günther, W., Hajak, G., 2013. Cognitive remediation improves cognition and good cognitive performance increases time to relapse – results of a 5 year catamnestic study in schizophrenia patients. BMC Psychiatry 13, 184.

Vita, A., De Peri, L., Barlati, S., Cacciani, P., Deste, G., Poli, R., Agrimi, E., Cesana, B.M., Sacchetti, E., 2011. Effectiveness of different modalities of cognitive remediation on symptomatological, neuropsychological, and functional outcome domains in schizophrenia: a prospective study in a real-world setting. Schizophr. Res. 133, 223–231.

Wykes, T., Reeder, C., Williams, C., Corner, J., Rice, C., Everitt, B., 2003. Are the effects of cognitive remediation therapy (CRT) durable? Results from an exploratory trial in schizophrenia. Schizophr. Res. 61, 163–174.

Wykes, T., Huddy, V., Cellard, C., McGurk, S.R., Czobor, P., 2011. A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. Am. J. Psychiatry 168, 472–485.

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