Computerised working-memory focused cognitive remediation therapy for psychosis — A preliminary study

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ABSTRACT

Background: Cognitive deficits are a core feature of schizophrenia and related psychotic disorders and are associated with decreased levels of functioning. Behavioural interventions have shown success in remediating these deficits; determining how best to maximise this benefit while minimising the cost is an important next step in optimising this intervention for clinical use.
Aims: To examine the effects of a novel working-memory focused cognitive remediation (CR) training on cognitive difficulties based on internet delivery of training and weekly telephone support.
Method: Participants with a diagnosis of psychosis (n = 56) underwent either 8 weeks of CR (approximately 20 h) or 8 weeks of treatment as usual (TAU). General cognitive ability, working memory and episodic memory were measured both pre and post intervention for all participants.
Results: In addition to improvements on trained working memory tasks, CR training was associated with significant improvements in two tests of verbal episodic memory. No association between CR and changes in general cognitive ability was observed. Effect sizes for statistically significant changes in memory were comparable to those reported in the literature based primarily on 1:1 training.
Conclusions: The cognitive benefits observed in this non-randomised preliminary study indicate that internet-based working memory training can be an effective cognitive remediation therapy. The successes and challenges of an internet-based treatment are discussed.

1. Introduction

A core feature of many psychotic disorders is poor cognitive performance. Deficits in cognition often predate the emergence of clinical symptoms, and then persist throughout the illness, strongly predicting functional outcome (Green et al., 2000; Wykes and Reeder, 2005). Because current antipsychotic medications do not adequately treat these deficits (Green, 1996; Fett et al., 2011), behaviour-based therapies designed to remediate cognitive deficits, an approach known as 'cognitive remediation' (CR), have become a significant focus of research.

CR has been used to refer to a number of interventions which seek to ameliorate difficulties with cognitive skills such as attention, memory, problem solving, information-processing speed, organisation, and planning. CR interventions differ widely in terms of method of administration (pen and paper versus computer), frequency of sessions, mode of administration (therapist-administered versus patient working alone) and method of training. Despite these differences, a meta-analysis by

Wykes et al. (2011) based on more than two thousand participants found consistent evidence of cognitive gains associated with CR, yielding an average effect size of ~0.5 across the range of interventions considered. Importantly, these benefits are not confined to cognition; CR has also been shown to be associated with benefits to social and occupational functioning (Wykes et al., 2011).

Several questions about CR remain, however, including the cost-effectiveness of the various approaches taken (Wykes, 2010). Even if the cost of CR compares favourably to currently used pharmacotherapy, the number of therapist hours involved are typically substantial, making delivery potentially problematic in standard clinical settings. Efforts to address this issue have included delivery of CR in a group setting (Medalia et al., 2001) and, recently, to make use of computer and/or internet-based approaches. While computerised approaches previously only permitted a 'one size fits all' approach, contemporary adaptive software enables task difficulty to be dynamically and automatically varied according to individual patient's response accuracy, and to changes in that response over time. This may permit patients the freedom to engage in training beyond the clinical setting and without the need of 1:1 support for each session. An important question for such 'e-health'

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Table 1
Number, age, chlorpromazine equivalent, gender and education of CR and TAU groups.

		CR group	TAU group	t/x^2	p
		N = 22	N = 26		
Psychosis subtype					
SZ		N = 14	N = 19		
SZA		N = 5	N = 5		
BP		N = 1	N = 1		
PDNOS		N = 2	N = 1		
Age	M (SD)	40.2 (8.8)	45.88(12.05)	−1.8	0.077
Chlorpromazine equivalent (mg/day)	M (SD)	495.7(515.7)	321.1(297.6)	1.1	0.278
Gender	M, F	17, 5	18, 8	0.503	0.478
Education: 1,2,3[a]	N in each respective category	7,9,6	10,7,9	5.74	0.57

[a] Education: 1, primary school education; 2, secondary school education; 3, post-secondary education.

initiatives is to determine patients' capacity to carry out such 'remote' training and how much training support is required to adequately facilitate participation.

A further question for maximising the cost effectiveness of training compares the benefits of a more general versus a more specific (and potentially shorter-term) approach to the cognitive functions being trained in CR. For example, working memory (WM) deficits have been exclusively targeted both in patients with schizophrenia (Lawlor-Savage and Goghari, 2014; Takeuchi et al., 2010) and in patients with other disorders (Klingberg, 2010; Richmond et al., 2011; Shipstead et al., 2012). This approach is partly based on the hypothesis that WM improvements may benefit cognitive function more generally. In support of this hypothesis, training programmes that exclusively focused on working memory in non-schizophrenia populations have been associated with a transfer of benefits to other cognitive functions including attention, problem-solving, and to fluid intelligence (Lilienthal et al., 2013; Salminen et al., 2012; Kundu et al., 2013; Rudebeck et al., 2012; Jaeggi et al., 2010; Jaeggi et al., 2008). To date, only a few studies have exclusively targeted WM training (particularly auditory WM) in psychosis. Results have been promising, with WM training being associated with improvements in both verbal WM and general cognitive ability (Fisher et al., 2009; Hubacher et al., 2013; Subramaniam et al., 2014; Wexler et al., 2000; Haut et al., 2010). Whether a targeted approach such as this is more beneficial, either in terms of size or cost effectiveness of effect, however, remains uncertain (Wykes et al., 2011).

The aim of this study was to investigate the effectiveness of a novel 8-week WM training programme, designed to be both ecologically valid and web-based, in patients with schizophrenia and related psychosis. In the preliminary phase of this study being reported here, we began to test this hypothesis by establishing whether cognitive performance improved in patients with psychosis who underwent CR training, and whether these changes differed from test-retest changes in clinically similarly patients receiving treatment as usual (TAU). Because WM is correlated with fluid intelligence, and WM training previously associated with gains in general cognitive ability (Jaeggi et al., 2010), we hypothesised that benefits to working memory capacity may lead to improvements in general cognitive ability.

2. Methods

2.1. CR participants

In the first stage of the study being reported here, 30 participants were recruited from community health teams from various sites across Ireland (Dublin, Wicklow, Sligo). Patients were referred by their local treatment teams following a series of presentations made about CR by the study team. All participants provided written informed consent and were interviewed using the Structured Clinical Interview for DSM-IV Axis 1 Disorders (SCID-I, First et al., 2002). DSM-IV diagnosis was established following a SCID interview and review of all available information — interview, family or staff report, and chart review. Criteria for inclusion in the study were that participants were aged between 18 and 65 years, had a history of psychosis, were community-based and clinically stable (in the opinion of the treating team), and were engaged in some activity (e.g. part time work or were attending a rehabilitation clinic for at least two days each week). Exclusion criteria included a history of organic impairment, head injury resulting in loss of consciousness, or drug abuse in the preceding 6 months.

2.1.1. Treatment as usual (TAU) participants

Immediately following the CR recruitment phase, a comparison group of 26 patient participants were ascertained from the same mental health services teams using the same inclusion and exclusion criteria as reported above. While these patients were therefore neither simultaneously collected nor randomly allocated, no differences in clinical or cognitive presentation were observed (see Table 1).

TAU consisted of multidisciplinary team input, including regular medical review, general psychosocial support from a community psychiatry nurse, and with additional inputs from occupational therapy and social work focusing on accommodation and occupation. Supportive group interventions (focusing on peer support and psychoeducation, and grounded in cognitive behavioural therapy principles) are available. While CBT for psychosis is also available on an individual basis, none of the patients in either the TAU or intervention conditions had received this in the six months before during or after participation in the study.

Table 2
Explanation of the 9 CR programme exercises and their relationship with the Baddeley Working Model.

Exercise		Baddeley Working Model
Faces snap	• A series of pictures of faces are shown, when two in a row appear, have to click	VSS[a] & WM
Spaces snap	• Square spaces are shown, when two appear in the same space, have to click	VSS & WM
Span colours	• A grid of four square of four colours flashes in a certain sequence, have to remember that sequence	VSS
Span colours reverse	• Same as above but sequence is entered in reverse	VSS & WM
Focus faces	• A series of faces are shown, have to remember the last two faces	VSS & WM
Double snap	• A combination of spaces snap and names snap (below)	VSS & PL & WM[b]
Names snap	• A series of names are heard, have to remember the last two	PL & WM
Span numbers	• A series of numbers are heard, have to type in all numbers at the end	PL
Span numbers reverse	• Same as above but are entered in reverse (last number to first heard)	PL & WM
Maths mad	• Number are called out and have to be added to 1-back (1, 4, 5 are called, 5 and 9 are entered)	PL & WM
Focus names	• A series of names are displayed and the last two names need to be remembered	PL & WM

[a] Visuo-spatial sketchpad.
[b] Phonological loop.

2.2. CR programme

An online CR training programme specifically targeting WM, developed by our group, was employed (McAvinue et al., 2013). This programme, which was web-based targeted both auditory and visual WM modalities following Baddeley's (2000) model. Each of the 9 training tasks was designed to be, to at least some extent, ecologically valid by relating training to every-day tasks (e.g. remember the faces of people introduced to you at a party) (see Table 2 and Fig. 1). Prior to commencing training, computer access and training needs of participants were evaluated. If the participants did not have internet access, a laptop and internet dongle were provided as was any training required with accessing the training website and logging on.

The programme consisted of a mixture of psycho-education on the nature of working memory, strategy-based learning, and practice of nine working memory focused training exercises that were gradually introduced over a 5-week period, beginning with the easier exercises first. The exercises ranged from n-back tasks to classic digit-span tasks while maintaining real-life similarities by using real faces and scenarios. For example, on one task (the Faces task, see Fig. 2), participants are given the scenario that they are at a party and asked to pay attention to the people they 'meet' at the party and are then later required to recollect the faces of the people they have been introduced to. During training, the exercises are adjusted in level of difficulty by changing the amount of information to be retained and the speed at which the information is presented, based on the participant's responses.

While the tasks themselves is primarily of the drill and practice variety, a strategy training component is also incorporated into the programme in both the online training and the weekly telephone support as follows: 1) before and after each practice session the applicability of individual WM tasks practised to real life situations are highlighted along with examples of how individual working memory strategies might be used in daily life; 2) during weekly phone calls, the therapist discussed with the participant how he or she applied these strategies, providing clarifications as needed and reinforcing the value of using these strategies. The strategies included techniques for exercise working memory day to day (e.g. attempting to remember phone numbers) and tips on how to organise information more effectively (e.g. learning how to use a mental blackboard). Details of the training exercises can be found in McAvinue et al. (2013).

Each participant was expected to practise the exercises for 30 to 40 min a day for 5 days a week (2 rest days — of the patient's choice).

Fig. 2. Example of an ecologically relevant exercise, focus faces.

In total, each participant was required to complete 40 days of training (30/40 min of training each day) within a 12-week window. If participants wished to complete more than the required 30 min of exercises a day, they were encouraged to do so. As part of the programme, at the end of each session participants were given visual feedback via a graph of time in training and scores obtained so that they could track their individual progress.

Assistance in completing the CR programme involved 1) an initial start-up session to demonstrate how the programme worked and 2) weekly phone calls to monitor and encourage progress. The phone calls incorporated a problem-solving based approach and motivational coaching. Participants were encouraged to identify solutions to any difficulties encountered. For example if a day of training was missed, participants were asked to identify the cause of the missed day and how to overcome these. For example, if the cause lay with technical difficulties, help was immediately provided to rectify the problem. If the cause was motivational, a more therapeutic approach was taken where difficulties were identified and deconstructed and help was given to find a solution and provide further encouragement. Participants were also provided with a detailed instruction manual and logbook to mark and keep track of their progress. Participants' activity was monitored regularly online, with the researcher having access to individual exercise performance, quantity of exercises completed and time and date of exercise completion.

2.3. Assessment of outcome

All CR & TAU patients completed the following outcome measures before and immediately after training (after 12 weeks in the case of TAU).
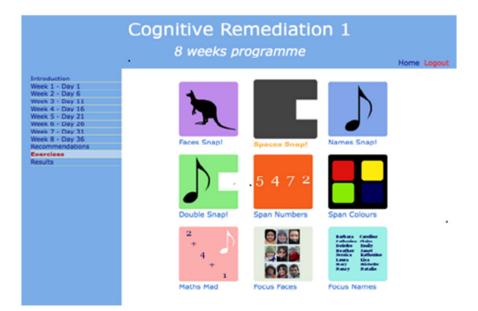

Fig. 1. Screen shot taken from the online training programme depicting the 9 CR exercises undertaken.

Episodic memory was assessed using the logical memory subtest from the Wechsler Memory Scale, 3rd edition (WMS-III; Wechsler, 1998). *Working memory* was assessed using letter number sequencing (LNS) from WMS-III.

Our primary outcome measures consisted of total scores on both the episodic memory and working memory tasks administered. To estimate whether any changes observed on any of the primary outcome variables related to more generalised effects on cognition, we also included two measures related to *general cognitive ability*. These were the Similarities and Matrix Reasoning subtests from the Wechsler Abbreviated Scale of intelligence (Wechsler, 1999).

2.4. Statistical analysis

We approached our analysis of the effects of CR on our main outcome variables as follows: First, demographic and clinical characteristics between the CR and TAU groups were compared using independent t-tests (for continuous data) and chi-squared (for categorical data) in SPSS 22.0 (IBM, 2013). Continuous variables included age and chlorpromazine equivalents, while categorical variables included gender and education. For each test run, group (two levels: CR and TAU) was entered as the grouping variable and the demographic characteristic in question was entered as the test variable. Next, the cognitive function of CR and TAU groups was compared at baseline using a general linear model, analysis of covariance (ANCOVA), in SPSS version 22. This was to ascertain whether any cognitive differences existed between the two groups prior to intervention. The cognitive variable was entered as the dependent variable with treatment group (CR V TAU) entered as the independent variable. Finally, association between intervention and cognitive function, episodic memory and working memory was tested using a general linear model in SPSS version 22 (SPSS, 2014). A mixed analysis of covariance (ANCOVA, repeated measures) was undertaken for each cognitive outcome variable. Treatment group (CR v. TAU) was used as the independent variable, stage (baseline assessment v. follow-up assessment) was used as the within-subjects variable, and baseline assessment was used as a covariate. Effect sizes of statistically significant associations were determined using Cohen's d, calculated using the means and standard deviations of the CR and TAU groups at post-intervention assessment. Calculations were conducted using the effect size generator found at www.ClinTools.com.

3. Results

3.1. Sample characteristics

A total of 56 participants were recruited, with an average age of 43.5 years, of whom 35 (76%) were male (see Table 1). There was a 27% (n = 8) withdrawal rate from the CR group following recruitment; various reasons for withdrawal were reported, including discomfort with using a PC and not having sufficient free time to complete the training. No significant differences between the groups (CR group n = 22, TAU group n = 26) were observed in gender ($x^2 = 0.503$, p = 0.478), medication dosage (chlorpromazine equivalents; t = 1.1, p = 0.278)

or education level ($x^2 = 5.74$, p = 0.57). For age, although not statistically significant, the TAU group trended towards being slightly older than the CR group (t = −1.8, p = 0.077 (see Table 1). Given the difference in age is 0.5 SD between the treatment groups, we ran the analysis with and without age as a covariate; no statistical difference in findings were observed between the two analyses. The results presented in Table 1 present the analyses run without co-varying for age.

3.2. Response to treatment intervention

A baseline comparison of the CR versus TAU groups revealed no significant differences between groups in cognitive performance, although a trend level difference in letter number sequencing performance was observed. At follow-up, by comparison, a number of significant differences emerged (see Table 3).

We next sought to establish whether any statistically significant differences were observed in the change from pre-assessment to post assessment. After co-varying for baseline differences in working memory, a trend level difference was observed between the CR group and the TAU group on working memory (letter number sequencing task; F = 3.14; p = .084). For episodic memory, patients in the CR group showed significantly greater improvements than the TAU group in episodic memory in both immediate and delayed recall paradigms (Logical memory I: F = 9.78; p = .003; Logical memory II: F = 6.69; p = .014; see Table 3). These differences represent medium sized effects according to Cohen's criteria (Logical memory I: Cohen's d = 0.46; Logical memory II: Cohen's d = 0.36). Finally, no difference was observed between treatment groups in general cognitive ability (WASI similarities: F = .062; p = .805, WASI Matrics: F = .071; p = .791, estimated full scale IQ (FSIQ): F = .338; p = .566). We observed no significant differences for the TAU group between pre and post measures on these tasks; by implication, the observed cognitive improvements in the CR group were unlikely to have been explained in terms of practice effects on these tasks.

As the amount of time participants spent engaged with the CR programme varied widely (mean minutes: 1030.2, SD minutes: 557; minimum 366.6 min, max 2592.3 min), we used Spearman's Rho to explore whether greater amounts of time engaged with the programme would result in greater cognitive improvements overall. No significant correlations were observed between total minutes and rate of change in performance following CR on any cognitive variable (all p > .05).

Only 5 subjects in total belonged to the Bipolar disorder (BD) and psychotic disorder not otherwise (PDNOS) specified groups (see Table 1). As SZ and BD differ in their profile of cognitive deficits to patients with SZ, we re-ran our analysis based on the SZ only cohort in order to compare results. Removing the BD and PDNOS patients from both the TAU and CR groups did not change the significance of the findings: the CR group continued to show significantly greater improvement over the TAU group in both immediate and delayed episodic memory (immediate: F = 10.32; p = 0.003; delayed: F = 6.07; p = 0.019) and trend level differences in rate of improvement in working memory (F = 3.0; p = 0.092).

Table 3
Comparing CR intervention group to TAU group on neuropsychological performance pre- and post-intervention using analysis of covariance.

	Pre-training				Post-training			
	CR	TAU	F	p	CR	TAU	F	p
Logical memory I	6.59 (3.34)	7.72 (3.7)	1.19	0.281	9.7 (3.37)	8.09 (3.63)	9.78	0.003
Logical memory II	7.4 (2.77)	7.8 (3.69)	0.164	0.687	9.38 (3.59)	8.09 (3.63)	6.69	0.014
Letter-number Sq	6.9 (3.29)	8.96 (3.94)	3.84	0.056	8.47 (2.52)	9.25 (3.89)	3.14	0.084
Estimated full scale IQ	96.1 (15.89)	90.73 (13.54)	1.1	0.301	99.05 (16.38)	91.18 (14.93)	0.338	0.566
Matrix reasoning	96.19 (19.6)	89.00 (13.19)	1.52	0.226	95.25 (22.01)	89.27 (17.12)	0.071	0.791
Similarities	97 (16.42)	93.53 (15.40)	0.41	0.526	96.8 (17.16)	93.18 (14.06)	0.062	0.805

4. Discussion

This study sought to ascertain the effectiveness of a novel 8-week WM training programme (completed within a 12-week window) on neuropsychological performance in patients with schizophrenia and related psychosis. Based on a comparison of patients receiving CR versus TAU, we observed 1) a trend-level association between CR training and improved performance on our primary outcome measure of working memory; 2) significant improvements in episodic memory as measured by the immediate and delayed conditions of the logical memory task. The effect sizes observed for these changes were moderate, consistent with estimates previously reported for CR (Wykes et al., 2011); and 3) the improvements in memory related tasks did not generalise to general cognitive functioning. These findings were unchanged when patients with psychotic disorders other than schizophrenia were removed from the analysis.

An important rationale for our study was determining the effectiveness and feasibility of a 'home-based' CR programme in which staff support was limited to telephone support ahead of carrying out a full randomised controlled trial. The findings from this preliminary study suggest that this approach is feasible: in stable community based patients, 74% were able to complete the programme using the telephone support available. Completers were defined by those having completed over 6 h (360 min) of the CR programme. Although still scarce, the literature evidences as little as 5 h of practice at sufficient intensity necessary to produced effects (McGurk et al., 2007; Wykes et al., 2011). These findings provide support for the approach taken, and echo other studies demonstrating the feasibility of 'home-based' computerised cognitive training programmes (Subramaniam et al., 2014; Ventura et al., 2013). As such, a randomised controlled trial of this intervention is warranted to establish the full benefits of this approach.

According to Wykes et al. (2011), one of the fundamental concepts of CR is that any cognitive benefits be generalisable across cognitive domains. A key finding of the current study is the transferability of cognitive benefit from WM training to episodic memory. This finding is in concordance with the literature where a positive association between WM and episodic memory performance in patients with psychosis has been reported (Kundu et al., 2013; Rudebeck et al., 2012). Two further cognitive domains have also been reported to be positively impacted by WM training; attentional ability (Kundu et al., 2013; Lilienthal et al., 2013) and fluid reasoning (Rudebeck et al., 2012; Jaeggi et al., 2008). Further investigation of these domains in relation to WM CR training would be desirable.

Unexpectedly, although WM specific CR proved significantly beneficial to episodic memory performance, training only resulted in trend level improvements in WM performance as measured by the letter number sequencing task when compared to TAU. This was despite the significant improvements on the nine working memory training tasks employed, and the significant change in letter number sequencing performance from pre to post training within the CR group. One explanation might be that many of the memory strategies taught in the CR programme were equally (if not more) relevant for episodic memory tasks than working memory tasks and that participants improved on the episodic memory tasks due to increased strategy use. However, this seems unlikely due to the CR tasks all being WM focused. A more likely explanation for this is our reliance on only one measure of working memory to assess outcome. This measure, which provided an index of verbal working memory, may not have been sufficiently sensitive to training related changes, given that our intervention focused on both visuospatial and auditory WM. A meta-analysis of WM training by Melby-Lervåg and Hulme (2013) of 23 studies suggested that WM training produces reliable short- and long-term improvements in WM skills for visuospatial WM but only weaker short-term improvements for verbal WM. Omission of a visuo-spatial measure of working memory was a short coming of this study and will need to be addressed before the true effects of this training on working memory can be established.

Furthermore, we did not test whether the benefits observed persisted over a longer period of time or whether a certain amount of "maintenance" training is required. This remains an area for investigation in future studies. Finally, and again in relation to measurements used, our reliance on a measure of general intelligence that did not specifically index fluid intelligence may similarly have resulted in a lack of sensitivity to detect additional training related changes.

As a preliminary study, a non-randomised comparison group (TAU) was employed, preventing us from making a definitive statement about the causality of the improvements. Limitations of the passive TAU comparison include the difference in study mediated social contact between the intervention and control groups. While the CR group was exposed to therapist contact during neuropsychological assessments, weekly phone calls and an initial in-person meeting to set up the programme, the control group met the therapist only for neuropsychological assessments. According to Ybarra et al. (2011), social interaction in and of itself may benefit cognition. In creating an active, rather than passive, control group, it may also be worth considering the inclusion of non CR specific computer games in order to ascertain whether it is the use of computers, rather than engagement with CR, that improves learning. A further limitation to the study is that assessors were not blinded to group condition, nor was group allocation randomly allocated. Blinding of raters has been associated with attenuated impacts observed for psychosocial interventions such as cognitive behavioural therapy as it minimises rater bias, and may have contributed to the effects observed in this study. To address these issues, a single-blind randomised controlled trial of our programme, employing an active placebo condition, and measuring training benefits on measures of real world functional outcomes as well as on cognition, is required and is currently underway.

In conclusion, the present study of a low-support computerised WM focused training programme, was associated with cognitive improvements in those patients who underwent training, with effects sizes comparable to those previously reported for other interventions. As noted, although promising these results are preliminary and require confirmation in an appropriately powered, randomised, blinded, controlled trial is required to confirm the validity of the cognitive benefits observed here.

References

Baddeley, A., 2000. The episodic buffer: a new component of working memory? Trends Cogn. Sci. (Regul. Ed.) 4, 417–423.
Fett, A.K., Viechtbauer, W., Dominguez, M.D., Penn, D.L., van Os, J., Krabbendam, L., 2011. The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: a meta-analysis. Neurosci. Biobehav. Rev. 35, 573–588.
First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B.W., 2002. Structured Clinical Interview for DSM-IV-TR Axis I Disorders. Research Version, Patient Edition. (SCID-I/P) New York: Biometrics Research, New York State Psychiatric Institute (November).

Fisher, M., Holland, C., Merzenich, M., Vinograd, S., 2009. Using neuroplasticity-based auditory training to improve verbal memory in schizophrenia. Am. J. Psychiatry 166, 805–811.

Green, M.F., 1996. What are the functional consequences of neurocognitive deficits in schizophrenia? Am. J. Psychiatry 153, 321–330.

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 (1), 119–136.

Haut, K.M., Lim, K.O., MacDonald, A., 2010. Prefrontal cortical changes following cognitive training in patients with chronic schizophrenia: effects of practice, generalization, and specificity. Neuropsychopharmacology 35, 1850–1859.

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

IBM Corp, 2013. IBM SPSS Statistics for Windows, Version 22.0. IBM Corp, Armonk, NY.

Jaeggi, S.M., Buschkuehl, M., Jonides, J., Perrig, W.J., 2008. Improving fluid intelligence with training on working memory. Proc. Natl. Acad. Sci. U. S. A. 105, 6829–6833.

Jaeggi, S.M., Studer-Luethi, B., Buschkuehl, M., Su, Y., Jonides, J., Perrig, W.J., 2010. The relationship between n-back performance and matrix reasoning-implications for training and transfer. Intelligence 38, 625–635.

Klingberg, T., 2010. Training and plasticity of working memory. Trends Cogn. Sci. 14 (7), 317–324 (Jul).

Kundu, B., Sutterer, D.W., Emrich, S.M., Postle, B.R., 2013. Strengthened effective connectivity underlies transfer of working memory training to tests of short-term memory and attention. J. Neurosci. 33, 8705–8715.

Lawlor-Savage, L., Goghari, V.M., 2014. Review: working memory training in schizophrenia and healthy populations. Behav. Sci. 4, 301–319.

Lilienthal, L., Tamez, E., Shelton, J.T., Myerson, J., Hale, S., 2013. Dual n-back training increases the capacity of the focus of attention. Psychon. Bull. Rev. 20, 135–141.

McAvinue, L.P., Golemme, M., Castorina, M., Tatti, E., Pigni, F.M., Salomone, S., Brennan, S., Robertson, I.H., 2013. An evaluation of a working memory training scheme in older adults. Front. Aging Neurosci. 5, 20 (May 23).

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 (12), 1791–1802.

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

Melby-Lervåg, M., Hulme, C., 2013. Is working memory training effective? A meta-analytic review. Dev. Psychol. 49 (2), 270–291 (Feb).

Richmond, L.L., Morrison, A.B., Chein, J.M., Olson, I.R., 2011. Working memory training and transfer in older adults. Psychol. Aging 26, 813–822.

Rudebeck, S.R., Bor, D., Ormond, A., O'Reilly, J.X., Lee, A.C., 2012. A potential spatial working memory training task to improve both episodic memory and fluid intelligence. PLoS One 7, e50431.

Salminen, T., Strobach, T., Schubert, T., 2012. On the impacts of working memory training on executive functioning. Front. Hum. Neurosci. 6, 166.

Shipstead, Z., Redick, T.S., Engle, R.W., 2012. Is working memory training effective? Psychol. Bull. 138, 628–65410.

SPSS, 2014. SPSS 22.0 Command Syntax Reference. SPSS Inc., Chicago.

Subramaniam, K., Luks, T., Garrett, C., Chung, C., Fisher, M., Nagarajan, S., Vinograd, S., 2014. Intensive cognitive training in schizophrenia enhances working memory and associated prefrontal cortical efficiency in a manner that drives long-term functional gains. NeuroImage 99, 281–292.

Takeuchi, H., Taki, Y., Kawashima, R., 2010. Effects of working memory training on cognitive functions and neural systems. Rev. Neurosci. 21 (6), 427–449.

Ventura, J., Wilson, S.A., Wood, R.C., Hellemann, G.S., 2013. Cognitive training at home in schizophrenia is feasible. Schizophr. Res. 143 (2–3), 397–398 (Feb).

Wechsler, D., 1998. Wechsler Memory Scale, Third edition (WMS-III). The Psychological Corporation, New York.

Wechsler, D., 1999. Wechsler Abbreviated Scale of Intelligence. The Psychological Corporation: Harcourt Brace & Company, New York, NY.

Wexler, B.E., Anderson, M., Fulbright, R.K., Gore, J.C., 2000. Preliminary evidence of improved verbal working memory performance and normalization of task-related frontal lobe activation in schizophrenia following cognitive exercises. Am. J. Psychiatry 157, 1694–1697.

Wykes, T., Reeder, C., 2005. Cognitive Remediation Therapy for Schizophrenia, Theory and Practice. Routledge, East Sussex.

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 (5), 472–485 (May).

Wykes, T., 2010. Cognitive remediation therapy needs funding. Nature 468 (7321), 165–166 (Nov 11).

Ybarra, O., Winkielman, P., Yeh, I., Burnstein, E., Kavanagh, L., 2011. Friends (and sometimes enemies) with cognitive benefits. What types of social interactions boost executive functioning? Soc. Psychol. Personal. Sci. 2 (3), 253–261 (May).