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**Computer-assisted cognitive remediation in patients with
schizophrenia: effects on symptoms, cognition and
psychosocial functioning.**

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Declaration of own work

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ABSTRACT

Background: Cognitive remediation is a behavioural intervention that aims to improve cognitive functioning with the goal of durability and generalisation. Although evidence suggests that computer-assisted cognitive remediation (CACR) improves cognitive functioning in individuals with schizophrenia, it remains unclear whether these effects generalise and lead to improvements in clinical symptoms and psychosocial functioning. The current study aimed to investigate the effects of CACR on clinical symptoms, cognitive functioning and psychosocial functioning in individuals with schizophrenia or schizoaffective disorder.

Method: A systematic review was performed using the quality assessment criteria defined by Scottish Intercollegiate Guidelines Network (SIGN 50) to investigate the effects of CACR on clinical symptoms in individuals with a diagnosis of schizophrenia or schizoaffective disorder. Additionally, a within subjects repeated measures design was used to investigate the effects of CACR on cognitive functioning, functional capacity and everyday social functioning.

Results: There was some evidence to suggest that CACR improves clinical symptoms, but the majority of studies reviewed did not report a significant effect, and a number of methodological weaknesses were identified in the literature. Results of the experimental study revealed improvements in speed of processing, reasoning and problem solving and the overall composite score for cognition, but these improvements could not be attributed solely to the CACR intervention. No improvements in functional capacity or everyday social functioning were observed.

Conclusions: Further, more rigorous research is required to develop a clearer understanding of the effects of CACR on clinical symptoms. The results of the experimental study support previous literature which has identified that a pure CACR intervention does not improve psychosocial functioning. The results are discussed in relation to the relevant literature.

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CHAPTER 1: SYSTEMATIC REVIEW

Running head: *Review of computer-assisted cognitive remediation in schizophrenia*

Title

A systematic review of the effects of computer-assisted cognitive remediation on clinical symptoms in individuals with schizophrenia or schizoaffective disorder.

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1.1 Abstract

Background: Cognitive remediation has been found to improve cognitive functioning, psychosocial functioning and clinical symptoms, in individuals with schizophrenia (McGurk et al., 2007). Recently, a review has demonstrated that computer-assisted cognitive remediation (CACR) improves cognitive functioning in individuals with schizophrenia (Grynszpan et al., 2011). The literature evaluating the effects of CACR on clinical symptoms has not yet been subject to a systematic review.

Method: A literature search was conducted to identify randomised controlled trials, investigating the effects of CACR on symptoms. A systematic review was then performed using the quality assessment criteria defined by Scottish Intercollegiate Guidelines Network (SIGN 50). Cohen's *d* was used to calculate effect sizes for each study, to evaluate the effectiveness of CACR at improving clinical symptoms.

Results: Fourteen studies met the inclusion criteria, and produced mixed results. Four studies reported a significant effect of CACR on symptoms. Eight studies, including the methodologically stronger studies, reported no significant effect on clinical symptoms. Clear conclusions were difficult to draw, due to a number of methodological weaknesses identified in the literature.

Conclusions: While there was some evidence for the effectiveness of CACR, methodologically stronger studies reported minimum benefits. Further studies that account for the methodological weaknesses of research in this area are needed in order to develop a clear evidence base about the effects of CACR on clinical symptoms.

Chapter 1 it is formatted according to the guidelines for *British Journal of Psychology* (Appendix 1)

1.2 Introduction

1.2.1 Schizophrenia

Schizophrenia is a severe mental illness characterised by profound disruptions in thinking, language, experience of emotions and perception (WHO, 2012).

Schizophrenia is thought to affect around 7 per 1000 individuals in the adult population, with the age of onset typically within the range of fifteen to thirty-five years of age (WHO, 2012). Schizophrenia is a notable cause of disability in developed countries, and during 2004/2005 the estimated total cost of schizophrenia in England, was 6.7 billion pounds (Mangalore & Knapp, 2007). Therefore, treatments to alleviate symptoms of schizophrenia and reduce disability in this population are of great clinical interest and may reduce the associated economic impact.

1.2.2 Clinical symptoms of schizophrenia

In the last two decades the symptoms of schizophrenia have been categorised into two distinct forms. Positive symptoms include delusions, hallucinations and disorganised speech, while negative symptoms include flattened affect, alogia, a loss of sense of pleasure, a loss of motivation and social withdrawal (Eaton et al., 1995). Treatments for symptoms associated with a diagnosis of schizophrenia include pharmacological interventions including typical and atypical antipsychotics and psychosocial interventions including family therapy and Cognitive Behavioural Therapy (NICE, 2009).

1.2.3 Cognitive deficits in schizophrenia

There is now substantial evidence supporting the view that impairment in cognition is a core feature of schizophrenia, which is present prior to disease onset and independent of clinical symptoms (Gold, 2004). Green et al. (2000) identified level of cognitive functioning as a greater predictor of outcome than clinical symptoms. Nuechterlein et al. (2004) reviewed evidence in this area and found that impairments in speed of processing, attention/vigilance, working memory, verbal memory, visual memory, problem solving and social cognition were frequently found in individuals with schizophrenia.

Research suggests that during the onset of symptoms, there is a period of notable decline in cognitive functioning, followed by a period of stabilisation (Medalia et al., 2009). Bilder *et al.* (2000) investigated cognitive functioning in patients with first-episode schizophrenia and found a large generalised deficit of 1.5 SD, compared to a healthy control group. Further to this finding, Heaton et al. (2001) reported that the level of cognitive impairment in individuals with schizophrenia remained stable, despite changes in clinical state both over a short-term period (mean 1.6 years) and long-term period (mean five years). These findings highlight that this population can have disabling cognitive deficits, which are pervasive and have a significant impact on both functioning and recovery.

The well documented presence of cognitive deficits in schizophrenia has resulted in suggestions that cognitive function should be included in the DSM-V, as a treatment-

relevant dimension, in order to highlight the importance of cognitive function in relation to functional status and clinical outcome (Barch & Keefe, 2010).

1.2.4 What is cognitive remediation

Wykes and Spaulding (2011) reported that a cognitive remediation experts' workshop defined cognitive remediation therapy (CRT) for schizophrenia as “a behavioural-training based intervention, that aims to improve cognitive processes (attention, memory, executive function, social cognition) with the goal of durability and generalisation” (p84). Within research in this field, a number of terms including cognitive rehabilitation and cognitive training have been used interchangeably. For the purposes of this review the term cognitive remediation will be used exclusively. Many forms of cognitive remediation have been developed and evaluated but there is a notable distinction between those that rely on non-computerised manual tasks, such as paper and pencil exercises, and those that are delivered in a more standardised manner via a computer training series.

Computer-assisted cognitive remediation (CACR) may have several advantages over some of the non-computerised tasks, as it offers a standardised training method that can provide immediate feedback and adapt to the current level of functioning of participants. Grynspan (2010) highlighted that CACR provides objective recording of performance and the use of computers promotes the acquisition of new compensatory strategies. Additionally, CACR can be delivered in a group format with minimum facilitators, which may provide a cost-effective alternative to face-to-face appointments with health

professionals. This approach may also be more appealing to patients who have difficulty engaging with health professionals.

1.2.5 Links between cognitive deficits, symptoms and poor outcome

In a meta-analysis of relevant literature, Green et al. (2000) identified associations between specific cognitive domains and functional outcome measures in individuals with schizophrenia. More specifically, secondary memory was linked with all outcome measures, immediate memory was linked with skill acquisition, executive function was linked with community functioning and vigilance was linked to skill performance (Green et al., 2000). Further studies have linked cognitive impairments to work performance (Bell et al., 2001), everyday functioning capacity (Twamley et al., 2002) and quality of life (Mohamed et al., 2008). These findings support the view that interventions aimed at improving cognitive functioning may in turn improve psychosocial functioning in individuals with schizophrenia.

Mohamed et al. (2008) highlighted that clinical symptoms, particularly positive symptoms, were related to quality of life. Additionally, Hunter and Barry (2011) found that negative symptoms showed strong and significant correlations with daily functioning, as assessed across a number of psychosocial outcome measures. This finding was supported by a literature review conducted by Green (1996), which reported that negative symptoms showed consistent associations with social problem solving and some weaker associations with community functioning. This evidence suggests that a greater severity of clinical symptoms is associated with poorer outcomes on numerous

assessments of psychosocial functioning; therefore, interventions that aim to reduce symptoms may also improve psychosocial functioning in individuals with schizophrenia.

Due to the demonstrated links between cognitive functioning, clinical symptoms and psychosocial functioning, it is of interest to develop the knowledge base regarding the effects of CACR on these three factors. In order to improve future treatments for individuals with schizophrenia, it is of particular interest to investigate whether a treatment that aims to improve cognitive functioning has any additional effects on symptoms and functioning.

1.2.6 Why do this review?

A number of reviews have evaluated the effects of cognitive remediation (Kurtz et al. 2001; Pilling et al. 2002; Krabbendam & Aleman, 2003; Twamley et al. 2003; McGurk et al. 2007). There is a growing body of literature supporting the use of cognitive remediation techniques to improve cognitive functioning in individuals with schizophrenia. McGurk et al. (2007) reported that cognitive remediation had a medium effect (0.41) for overall cognition, a small to medium effect (0.35) for functioning and a small effect (0.28) for symptoms. Cognitive remediation has also been found to have a greater effect on psychosocial functioning when offered in addition to psychiatric rehabilitation (McGurk et al., 2007). Although this review provided promising findings to support the use of cognitive remediation, its analysis did not distinguish between

computer-assisted methods and more traditional techniques; therefore, no conclusions could be drawn about the comparative effectiveness of each method of delivery.

As previously discussed, CACR may have several advantages over some of the non computerised approaches, as it provides a standardised training method that can give immediate feedback and adapt to the current level of functioning of the participant.

Grynszpan et al. (2011) reported results in line with previous reviews of cognitive remediation; reporting that CACR had an effect size of 0.38 on general cognition.

Additionally, this study found that interventions targeting specific cognitive domains did not produce higher effects than those using non-domain specific interventions

(Grynszpan et al., 2011). Although this provided evidence to support the use of CACR to improve cognitive functioning in individuals with schizophrenia, it did not evaluate the effects of CACR on symptoms or psychosocial functioning. A growing body of literature has investigated the effects of CACR on clinical symptoms, but to date this literature has not been reviewed and therefore it remains unclear whether CACR can improve clinical symptoms.

McGurk et al. (2007) conducted a review of controlled studies evaluating the effects of cognitive remediation on clinical symptoms in individuals with a diagnosis of schizophrenia or schizoaffective disorder. This study found that cognitive remediation had a small effect on clinical symptoms, therefore, it was hypothesised that CACR would improve clinical symptoms as assessed by standardised measures.

1.3 Method

The review was conducted in a manner consistent with the guidance for undertaking systematic reviews set out by the Centre for Reviews and Dissemination (2009). These guidelines are internationally recognised, and are recommended by the National Institute for Health and Clinical Excellence (NICE). In the current review, the effects of CACR on clinical symptoms were established by calculating effect sizes across time of the differences between the CACR and control groups.

1.3.1 Procedure

Prior to undertaking the systematic review, a literature search was undertaken to identify previous reviews of CACR in schizophrenia. The Cochrane Database of Systematic Reviews (CDSR) and the Database of Abstracts and of Reviews of Effects (DARE) were searched, in addition to a wider search of online databases. This process identified one systematic review, conducted by Grynszpan et al. (2010), relevant to the research topic. Grynszpan et al. (2010) evaluated the efficacy of CACR in relation to associated effects on cognitive functioning, but did not evaluate any effects on other factors such as clinical symptoms or psychosocial functioning. It was therefore identified that a systematic review evaluating the efficacy of CACR on either of these outcome measures would be a beneficial addition to the existing literature.

1.3.2 Literature search procedure

Studies for the systematic review were identified through literature searches for English

language articles that were published in peer-reviewed journals in four online databases.

The following electronic databases were searched up to the end of February 2012:

- PsychINFO (from 1990)
- MEDLINE (from 1946)
- Embase (from 1980)
- CINAHL (from 1937)

The literature search combined the following keywords: ‘schizophrenia’ or ‘schizoaffective disorder’ AND ‘cognitive training’ or ‘attention training’ or ‘cognitive remediation’ or ‘cognitive rehabilitation’ AND ‘computer-assisted’. The reference list of each selected article was then scanned to identify any additional articles. Table 1.1 provides a summary of results obtained from all sources. The literature search produced 371 potential papers, 14 of which were included in the current review. A detailed breakdown of the literature search procedure can be seen in Figure 1.1.

1.3.3 Inclusion and exclusion criteria

Studies that met the following criteria were included in the current systematic review:

- 1) A randomised controlled trial investigating the benefits of CACR using a pre/post design.
- 2) A pre/post assessment of clinical symptoms using at least one standardised measure.
- 3) A sample that consisted of adult participants, exclusively with a diagnosis of either schizophrenia or schizoaffective disorder.

In summary, studies were eligible for inclusion if they were randomised controlled trials, investigating the effects of CACR in an adult population with a diagnosis of schizophrenia or schizoaffective disorder, using a pre and post-design that included at least one validated outcome measure of clinical symptoms.

Table 1.1: Summary of literature sources

Source of articles	Number of potential articles identified for screening
PsychINFO	34
EMBASE	33
CINAHL	7
Medline	19
Articles from database search after duplicates removed	70
Articles identified through additional reference sources	301
All sources	371

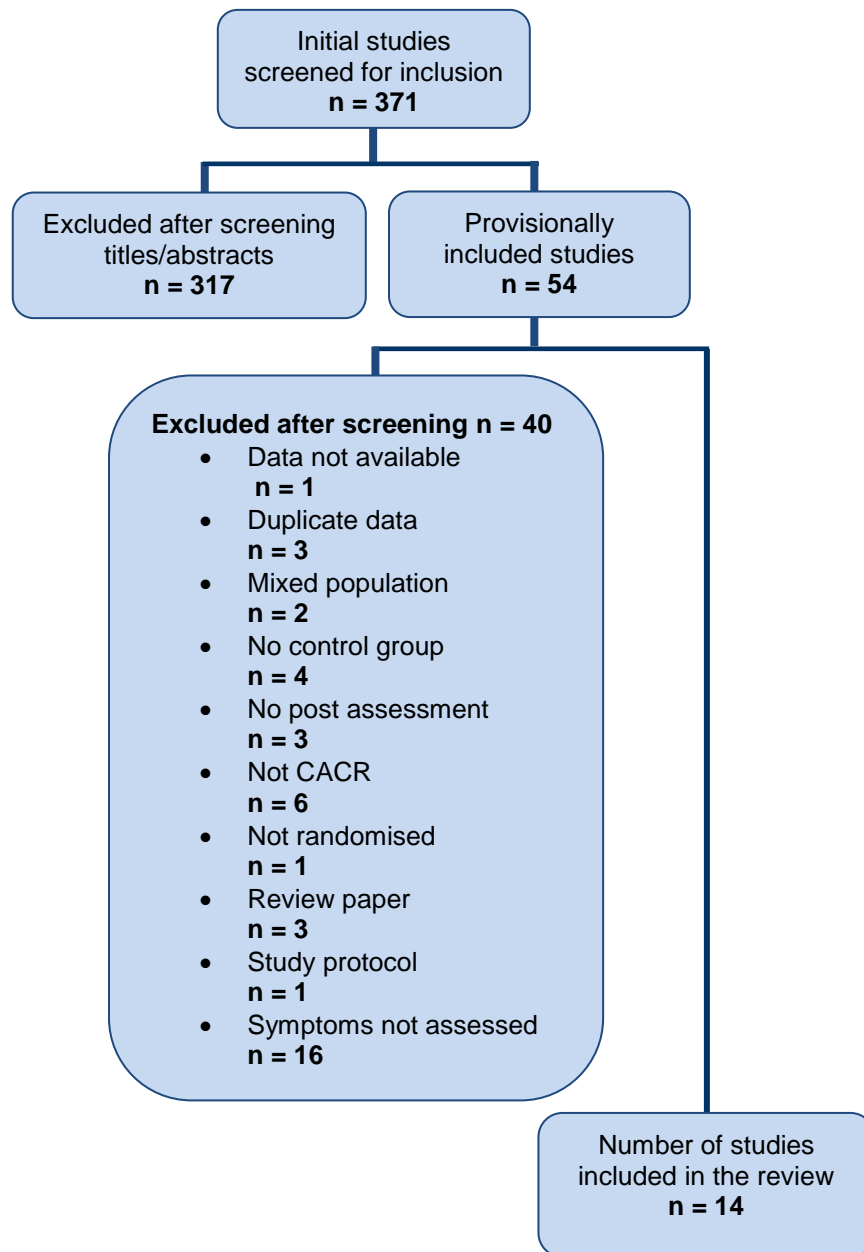
1.3.4 Population

The studies included in the review were based exclusively on adult participants with a diagnosis of either schizophrenia or schizoaffective disorder.

1.3.5 Intervention

Because of the limited number of clinical symptoms outcome studies in this area, all studies that used CACR were considered for the current review. The studies included in the review used a variety of interventions; some relied on a pure CACR intervention while others used CACR as part of a wider intervention.

Figure 1.1: Flow chart detailing the study selection process



1.3.6 Comparators

Studies were eligible for inclusion if they compared a form of CACR (either a pure CACR intervention or CACR as part of the intervention) to either a treatment as usual

condition (TAU), active control condition (e.g. computer games) or passive control condition (e.g. waiting list control).

1.3.7 Outcome measures

Studies assessing clinical symptoms pre and post-intervention through validated self report and/or observer rated measures were included in the current review. Where the pre and post-assessment scores were not reported in the article the authors were contacted requesting this data.

1.3.8 Statistics

Cohen's *d* values measuring the effect sizes between CACR and control conditions were calculated using the means and standard deviations of symptom outcome measures reported in the papers. Where this data was not reported, the authors were contacted requesting this information. Morris (2008) evaluated methods for establishing effect sizes in pre-post test designs and concluded that the effect size should be calculated using both the pre-test and post-test information in order to take full advantage of all the information available. Morris (2008) recommended using the mean change from pre-test to post-test in the experimental and control group, divided by the pooled pre-test standard deviation. This method was employed in the current review and for each study the effect size was calculated for every symptom outcome measure used.

1.3.9 Assessment of quality of included studies

The quality of the studies included in the current review was evaluated using the Scottish Intercollegiate Guidance Network (SIGN) methodology checklist for randomised controlled trials. Each study was rated and scored on the 10 quality criteria using the outcome ratings recommended by SIGN: ‘well covered’ (2); ‘adequately addressed’ (1); and ‘poorly addressed’, ‘not reported’ and ‘not applicable’ (all 0), to allow an overall comparison between studies. A detailed breakdown of the scoring criteria used in the current review can be found in appendix 2. Five of the studies included in the current review were independently rated by S.O on the 10 quality assessment criteria to ensure consistency in the ratings. The reviewers (J.M & S.O) found agreement on 78 per cent of the quality assessment criteria. Where differences were found, these were reviewed and amended appropriately.

1.4 Results

From the 371 studies identified by the original literature search, 317 were excluded after screening the titles and abstracts, as they did not meet the inclusion criteria for the current review. A further 40 articles were excluded after a more detailed screening of the articles was undertaken (appendix 3). A total of 14 studies, comprised of 983 participants, met the inclusion criteria for the current review. The outcome measure scores from a total of four studies (Cavallaro et al., 2009; Hogarty et al., 2004; Hodge, 2010; Galderisi, 2010) were not available and therefore effect sizes were calculated for the remaining 10 studies. The characteristics of the included studies, a summary of the main findings and their associated effect sizes can be seen in Table 1.2.

Table 1.2. Characteristics, main findings and effect sizes of reviewed studies

Authors	Population (n)	Sample Characteristics		Follow-up (months)	Intervention characteristics	Symptoms outcome measure	Summary of relevant results	Effect size for CACR on symptoms measures
		Experimental	Control					
Belluci et al. (2003)	Schizophrenia (16) Schizoaffective disorder (18)	Captain's log software (17)	Passive: Waiting list control (17)	None	2 half hour sessions per week for 8 weeks	SANS SES	The CACR group demonstrated significantly greater reduction from pre to post test scores on 3 of 5 SANS subscales and the global SANS score.	SANS summary d = 0.70 SANS subtests d = 0.24 - 0.66
Cavallaro et al. (2009)	Schizophrenia (86)	Domain specific training using Cogpack software plus standard treatment (50)	Active: Non domain specific CACR plus standard treatment (36)	None	3 1-hour sessions per week for 12 weeks (total of 36 hours)	PANSS	Clinical symptoms remained unchanged between the two groups throughout all the observations	Data not available
d'Amato et al. (2011)	Schizophrenia (77)	RehaCom software (39)	Passive: Waiting list control (38)	None	14 2-hour sessions over 7 weeks	PANSS GCI	No improvements in positive or negative symptoms as measured by the PANSS or the CGI	PANSS Positive d = 0.06 PANSS Negative d = -0.25 PANSS General d = 0.02
Dickinson et al. (2010)	Schizophrenia (49) Schizoaffective disorder (14)	Unspecified CACR (34)	Active: Computer work (27)	3-month follow up	3 per week for 15 weeks (maximum of 36 sessions)	BPRS SANS	No significant effects on any symptom outcome measure post or follow up.	BPRS d = -0.19 SANS d = -0.10
Eack (2009)	Schizophrenia (38) Schizoaffective disorder (20)	Computer assisted training in attention, memory and problem solving (31)	Active: Enriched supportive therapy (27)	No follow up using symptom outcome measure	Approximately 60-hours of weekly CACR and 45 social cognition group sessions over two years	BPRS; Wing negative symptoms scale; Raskin depression; Covi anxiety; patient subjective response questionnaire	CACR had significant and medium to large differential improvements in symptomatology compared to EST	Symptoms year 1 d = 0.55 Symptoms year 2 d = 0.82

Hogarty et al. (2004)	Paranoid schizophrenia (68),	Cognitive enhancement therapy (67)	Active: Enriched supportive therapy (54)	1-year Follow-up	75 hours of progressive software training	BPRS; Wing negative symptoms scale; Raskin depression scale; Patient subjective response questionnaire	No significant effect on symptoms at year 1 or 2	Data not available
Hogarty et al. (2006)	Schizoaffective disorder (36) Other schizophrenia (17)							
Vita et al. (2011)	Schizophrenia (90)	IPT cog (26) and CACR using Coppack software (30)	Active: Psychosocial intervention (28)	None	2 45 minute sessions per week for 24 weeks	PANSS CGI-S	Significant improvement in PANSS scores in CACR group compared to control	CGI-S d = 0.53 PANSS positive d = 0.58 PANSS negative d = 0.64 PANSS total d = 0.85
Wolwer et al. (2005)	Schizophrenia (77)	Computerised affect recognition training (28) and CACR using Cogpack software (24)	Passive: TAU (25)	None	2 45 minute sessions per week (12 in total)	PANSS	Effects on clinical symptoms not reported in analyses	PANSS negative d = 0.09 PANSS positive d = 0.10 PANSS total d = 0.16
Fisher et al. (2009)	Schizophrenia (55)	Computerised auditory information processing training (29)	Active: Computer games (26)	6-month follow up	1 hour sessions, number of weeks not specified	PANSS	No significant interaction of condition or time and no significant main effect of condition or time on PANSS scores	PANSS positive d = -0.07 PANSS negative d = -0.12 PANSS total d = -0.11
Hodge (2010)	Schizophrenia Schizophreniform disorder Schizoaffective disorder Ns not specified	NEAR (22)	Passive: Waiting list control (18)	4-month follow up	2 1-hour session per week for 10-15 weeks (20-30 session in total)	PANSS CDS	No significant change in PANSS or CDS scores from baseline to post treatment or at 4-month follow up	Unable to compute (scores not reported separately).

Hermanutz & Gestrich (1991)	Schizophrenia	Computerised attention training (10) and social training (10)	Passive: TAU (10))	None	15 sessions over 3-4 weeks	BPRS GAS PD scale of von Zerssen	Improvements in symptoms in all 3 groups. No difference between groups	BPRS anxiety/depression d = -0.12 , BPRS anergia d = -0.13 , BPRS thought disturbances d = 0.18 , BPRS activation d = 0.30 , BPRS hostility d = 0.55 , PD-S hostility d = 0.19 PD-S depression d = 0.31
Medalia (1998)	Schizophrenia (54)	ORM (27)	Active: Watched documentaries (27)	None	18 sessions over 6 weeks	BPRS	Both groups showed significant change on BPRS, but CACR group improved significantly more	BPRS d = 0.27
Vauth (2005)	Schizophrenia (138)	CACR plus vocational rehab (45) and TSSN (35)	Active: Vocational rehab alone (46)		2 90-minute sessions twice a week for 8 weeks	PANSS CDS SHAPS-D	No significant difference was found for TSSN in improvements of negative symptoms	PANSS negative d = -0.41 SHAPS-D anticipatory anhedonia d = 0.54
Galderisi (2010)	Schizophrenia Schizoaffective disorder (Not specified)	Social skills training plus individualised CACR using ReHaCom software (30)	Active: Structured leisure activities (30)	None	2 1-hour sessions per week for 26 weeks (48 hours)	SANS SAPS	No interaction time x group x clinical symptoms dimension x group was observed.	Data not available

Note: - BPRS: Brief psychiatric rating scale; CACR: Computer assisted cognitive remediation; CDS: Calgary depression scale; GCI: Clinical global impression; CGI-S: Clinical global impression severity; GAS: Global Assessment Scale; IPT: Integrated Psychological Therapy; NEAR: Neuropsychological Educational Approach to Remediation; ORM: The Orientation Remedial Module; PANSS; positive and negative symptoms scale; SAPS: Scale for the assessment of positive symptoms; SANS; Scale for the assessment of negative symptoms; SES: Self-esteem scale; SHAPS-D: German version of the Snaith-Hamilton Pleasure Scale. TAU; Treatment as usual; TSSN: Training of self-management skills for negative symptoms.

1.4.1 Quality of included studies

Table 1.3 provides ratings for each of the 14 studies on the SIGN quality criteria, which offers a guide to the studies' methodological strengths and weaknesses. It indicates that Dickinson et al. (2010) conducted the strongest study methodologically, while Hogarty et al. (2004) and Hermanutz & Gestrich (1991) carried out the weakest. There was variation in the control conditions used across the studies. Of the studies included in the current review, nine used an active control condition such as computer work (Cavallaro et al., 2009; Dickinson et al., 2010; Fisher et al., 2010); enriched supportive therapy (Eack, 2009; Hogarty et al., 2004); psychosocial intervention (Vita et al., 2011); nature documentaries (Medalia, 1998); vocational rehabilitation (Vauth, 2005) or structured leisure activities (Galderisi, 2010). The remaining five studies used a passive control condition such as a waiting list control (Belluci et al., 2003; D'Amato et al., 2011; Hodge, 2010) or treatment as usual (Wolwer et al., 2005; Hermanutz & Gestrich, 1991).

All studies included in the current review were scored as having an 'adequately addressed' or 'well covered' focused question relating to their research. It should be noted that the effect of CACR on symptoms was frequently not one of the primary research questions and one study (Wolwer et al., 2005) did not discuss any effects on symptoms, however, it included sufficient data to be included in the current review. All studies included in the current review used some form of randomisation in their methodology. Five studies gave detailed descriptions of their method of randomisation (Dickinson et al., 2010; Eack, 2009; Hogarty et al., 2004; Vita et al., 2011; Hodge, 2010)

while the remaining nine studies simply stated that participants were randomised to conditions.

Only four studies explicitly used some form of adequate concealment at the start of their study (d'Amato et al., 2011; Fisher et al., 2010; Hodge, 2010 and Galderisi, 2010). The remaining nine studies did not provide sufficient information to assess whether the researchers were unaware of participant group allocation at the time they entered the study. Further to this, only five studies ensured assessors were fully blind to the participant group allocation when conducting the outcome assessments (D'Amato et al., 2011; Vita et al., 2011; Fisher et al., 2010; Vauth, 2005 and Galderisi, 2010) and only one study (Belluci et al., 2002) ensured that participants were blind to their treatment group throughout the study.

All studies included in the review considered whether the groups were similar at the start of their research and were scored 'well covered' or 'adequately addressed' on this quality criterion. Two papers (Belluci et al., 2003 and Dickinson et al., 2010) stated that the treatment under investigation was the only difference between groups. It was unclear in a further two papers (Eack, 2009 and Hogarty et al., 2004) whether the treatment was the only difference. In the remaining ten studies it seemed likely that the treatment was the only difference, however, this was not explicitly stated.

Five studies used robust outcome measures that are intended for use with this population (Cavallaro et al., 2009; d'Amato et al., 2011; Eack, 2009; Hogarty et al., 2004 and

Fisher et al., 2010); the remaining studies all used standardised measures that were not designed specifically for use with this population. Four studies failed to include sufficient information about dropout rates in their papers (Belluci et al., 2003; d'Amato et al., 2011; Eack, 2009 and Hermanutz & Gestrich, 1991).

Only three studies included in this review clearly stated that intention to treat analyses were carried out (Dickinson et al., 2010; Eack, 2009 and Wolwer et al., 2005). Although many of the studies are likely to have conducted intention to treat analyses, it was not clearly stated in the papers.

1.4.2 Effects on symptoms

When effect sizes were not reported for symptom outcome measures for the intervention and control groups, they were calculated using Cohen's *d*. The effects of CACR on clinical symptoms varied considerably across studies. Of the papers included in the current review, only one study used an intention to treat analysis (Eack, 2009). Four studies reported that compared to the control condition, CACR had a significant effect on clinical symptoms as assessed by a standardised measure (Belluci et al., 2003; Eack, 2009; Vita et al., 2011; Medalia, 1998). Belluci et al. (2003) reported that CACR was found to significantly reduce scores on the Scale for the Assessment of Negative Symptoms (SANS) on three of the five subscales as well as the SANS total score. Belluci et al. (2003) noted that CACR resulted in small to medium effect sizes on the SANS subscales and total score ($d = 0.24 - 0.70$). Eack (2009) reported that compared

to enriched supportive therapy, CACR significantly improved symptoms as defined as a composite score, with a medium effect at year 1 ($d = 0.55$) and a large effect at year 2 ($d = 0.82$). Vita et al. (2011) reported that compared to a psychosocial intervention, CACR significantly improved symptoms with a medium effect ($d = 0.53$) as assessed by the Clinical Global Impression-Severity (CGI-S) scale and with medium to large effects ($d = 0.58 - 0.85$) as assessed by the Positive and Negative Syndrome Scale (PANSS). Medalia (1998) reported that CACR significantly improved symptoms, as assessed by the Brief Psychiatric Rating Scale (BPRS), with a small effect ($d = 0.27$).

Eight studies, including the four with the highest quality assessment rating scores, reported that CACR did not have a significant effect in comparison to control conditions on clinical symptoms (Cavallaro et al., 2009; d'Amato et al., 2011; Dickinson et al., 2010; Hogarty et al., 2004; Fisher et al., 2010; Hermanutz & Gestrich, 1991; Hodge, 2010; Galderisi, 2010). It is worth noting that Hermanutz & Gestrich (1991) found improvements in symptoms in all three groups in their study, but the CACR group had associated small to medium effects on symptoms as assessed by the BPRS, GAS and the von Zerssen scale.

A further two studies did not report the effects of CACR on symptoms, however, they provided sufficient information about symptom outcome measure scores, to be included in this review (Wolwer et al., 2005; Vauth, 2005). When Cohen's d effect sizes were calculated for these studies, mixed results were obtained. The study by Wolwer et al. (2005) resulted in effect sizes ranging from 0.09 for the PANSS negative subscale, 0.10

for the PANSS positive subscale and 0.16 for the PANSS total score. These findings indicate that CACR did not have a clinically meaningful effect on clinical symptoms.

Vauth (2005) investigated the effects of a comparison group on clinical symptoms, but did not investigate the effects of CACR on the clinical symptoms outcome measures.

Vauth's (2005) study resulted in effect sizes ranging from -0.41 for the PANSS negative subscale to 0.54 for the German version of the Snaith Hamilton Pleasure Scale (SHAPS-D) anticipatory anhedonia subscale. These findings provide some evidence that CACR has a medium effect on anticipatory anhedonia, and therefore may be of clinical benefit.

Table 1.3: Quality assessment criteria as defined by SIGN-50 guidelines

Study	1.1 Clarity of question	1.2 Randomised	1.3 Adequate concealment	1.4 Blinded	1.5 Groups similar at start	1.6 Treatment only difference	1.7 Relevant outcome measures	1.8 Drop out %	1.9 Intention to treat analysis	1.10 Comparable results across sites	Quality score
Belluci et al. (2003)	WC 2	AA 1	NR 0	WC 2	AA 1	WC 2	AA 1	NA 0	PA 0	N/A 0	9
Cavallaro et al. (2009)	AA 1	AA 1	NR 0	PA 0	WC 2	AA 1	WC 2	14% WC 2	PA 0	NA 0	9
D'Amato et al. (2011)	WC 2	AA 1	AA 1	AA 1	WC 2	AA 1	WC 2	NA 0	PA 0	NA 0	10
Dickinson et al. (2010)	WC 2	WC 2	NR 0	PA 0	WC 2	WC 2	AA 1	11% WC 2	WC 2	AA 1	14
Eack (2009)	WC 2	WC 2	NR 0	PA 0	WC 2	PA 0	AA 1	NR 0	WC 2	N/A 0	9
Hogarty et al. (2004)	AA 1	AA 1	NR 0	NA 0	AA 1	PA 0	AA 1	12% WC 2	AA 1	N/A 0	7
Vita et al. (2011)	WC 2	WC 2	NR 0	AA 1	WC 2	AA 1	AA 1	2% AA 1	PA 0	N/A 0	10
Wolwer et al. (2005)	WC 2	AA 1	NR 0	NR 0	WC 2	AA 1	AA 1	31% WC 2	WC 2	N/A 0	11
Fisher et al. (2010)	WC 2	AA 1	AA 1	WC 2	WC 2	AA 1	WC 2	37% WC 2	PA 0	N/A 0	13
Hermanutz & Gestrich (1991)	AA 1	AA 1	NR 0	NR 0	AA 1	AA 1	AA 1	NR 0	PA 0	N/A 0	5
Hodge (2010)	WC 2	WC 2	AA 1	PA 0	WC 2	AA 1	AA 1	42% WC 2	NA 0	NA 0	11

Study	1.1 Clarity of question	1.2 Randomised	1.3 Adequate concealment	1.4 Blinded	1.5 Groups similar at start	1.6 Treatment only difference	1.7 Relevant outcome measures	1.8 Drop out percentage	1.9 Intention to treat analysis	1.10 Comparable results across sites	Quality score
Medalia (1998)	WC 2	AA 1	NR 0	PA 0	WC 2	AA 1	AA 1	10% WC 2	PA 0	N/A 0	9
Vauth (2005)	WC 2	AA 1	NR 0	AA 1	WC 2	PA 0	AA 1	28% WC 2	WC 2	N/A 0	11
Galderisi (2010)	WC 2	AA 1	AA 1	AA 1	WC 2	AA 1	AA 1	36% WC 2	PA 0	N/A 0	11
Total scores	25	18	4	8	25	13	17	19	9	2	

Note: WC: well covered, AA: adequately addressed, PA: poorly addressed, NA: not addressed, NR: not reported, N/A: not applicable.

Quality criteria

- 1.1) The study addresses an appropriate and clearly focused question.
- 1.2) The assignment of subjects to treatment groups is randomised.
- 1.3) An adequate concealment method is used.
- 1.4) Subjects and investigators are kept 'blind' about treatment allocation.
- 1.5) The treatment and control groups are similar at the start of the trial.
- 1.6) The only difference between groups is the treatment under investigation.
- 1.7) All relevant outcomes are measured in a standard, valid and reliable way.
- 1.8) What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out?
- 1.9) All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).
- 1.10) Where the study is carried out at more than one site, results are comparable for all sites

1.5 Discussion

The current systematic review aimed to review previous research to evaluate the effectiveness of CACR in improving clinical symptoms in individuals with a diagnosis of schizophrenia or schizoaffective disorder. There were differences in the methodologies of the studies included in the current review. The majority of the studies reviewed failed to report whether an adequate form of concealment was used in their study. In addition to this, most studies were weakened by their failure to ensure that assessors and participants were blind to group allocation. Such weaknesses in the research need to be addressed and there is a need for further, more rigorous research, which uses adequate concealment and employs appropriate blinding techniques.

There were inherent differences in interventions offered both as treatment and control conditions by the studies included in the current review. This resulted in the interpretation of results being somewhat difficult. Some studies made use of an active control condition, whilst others made use of a passive control condition. Additionally, some studies used CACR as part of a wider intervention, while other studies used a pure form of CACR as the sole intervention. Although it would have been beneficial to conduct a review investigating the effects on symptoms of either a pure CACR intervention or the use of CACR as part of a wider intervention, the limited number of studies in this area meant it was not feasible and both intervention strategies were taken into account for this current review.

Of the fourteen papers included in the current review, four reported a significant effect of CACR on clinical symptoms, as assessed by a standardised measure. These four studies were of similar quality as assessed by the quality criteria, but it is worth noting that a number of studies that were deemed to be stronger methodologically did not report a significant effect of CACR on clinical symptoms.

Three of the four studies that reported significant effects of CACR on clinical symptoms offered a pure CACR intervention. Additionally, the studies that found significant effects all used measures developed for specific use with this population. However, it is also worth noting that the same measures were employed in some of the studies that did not report an effect, but were considered stronger methodologically. Five of the eight studies (Fisher et al., 2009; Hermanutz & Gestrich, 1991; Dickinson et al., 2010; Cavallaro et al., 2009; D'Amato et al., 2011) that did not report a significant effect of CACR on clinical symptoms offered a pure CACR intervention programme.

The results of this review do not provide enough evidence to conclude that CACR has a specific effect on clinical symptoms. Although four studies reported significant effects of CACR on clinical symptoms (ranging from small to large effect sizes), eight studies, including those with the strongest methodology, did not find any significant effects.

1.5.1 Strengths of the review

The current article aimed to review an area of clinical importance and to answer a question that has not been reviewed previously. Additionally, the current systematic review also aimed to be as pure as possible, by excluding studies that included individuals with diagnoses other than schizophrenia or schizoaffective disorder.

Where necessary data was not available from journal articles, primary and secondary authors were contacted to request this data. A high level of inter-rater reliability was found in the journal articles, which were reviewed by two independent people (J.M & S.O), suggesting consistency of the quality criterion ratings.

1.5.2 Limitations of the review

Due to a lack of translation resources, the current systematic review was limited to articles published in English and it was acknowledged that a number of German articles may have been eligible for inclusion. Despite a growing interest over recent years in the effects of CACR, the relatively small numbers of studies investigating the effects of CACR on clinical symptoms resulted in studies with a variety of treatments and measures being included in the current review. As more research is published in this area, it would be beneficial to conduct a further review, drawing comparisons between studies that used a pure CACR intervention and those that used CACR as part of a wider intervention.

1.5.3 Implications for clinical work and future research

Although there is strong evidence demonstrating the clinically beneficial effect of CACR on cognitive functioning, the current review demonstrates that there is

insufficient evidence to conclude that CACR is effective at improving clinical symptoms in individuals with a diagnosis of schizophrenia or schizoaffective disorder, and that additional treatments will need to be considered to improve clinical symptoms in this population.

One of the main goals of offering CACR is the hope that any effect will generalise to psychosocial functioning and thereby, reduce disability and improve quality of life in this population. A number of studies have investigated the effects of CACR on psychosocial functioning and a comprehensive review of this area of interest would be beneficial. Additional studies further investigating the benefits of CACR on cognitive functioning, psychosocial functioning and clinical symptoms are required to expand the knowledge base in this field and develop a clearer understanding about the efficacy of CACR.

1.6 Conclusions

This systematic review of the effects of CACR on clinical symptoms, in individuals with a diagnosis of schizophrenia or schizoaffective disorder found insufficient evidence to draw firm conclusions about an effect. While a number of papers did demonstrate small to large effects of CACR on clinical symptoms ($d = 0.25 - 0.82$), the methodologically stronger papers did not report a significant effect. It should be noted that the majority of papers in this area had a number of key weaknesses that should be addressed by future research. Future research needs to be rigorous and give consideration to the following key areas:

- 1 Ensuring an adequate concealment method is employed to ensure researchers are not aware of participant group allocation at the start of the research.
- 2 Employing a double blind design where possible, or ensuring that at least the assessors are blind to participant group allocation.
- 3 Ensuring that control groups are well matched in order to certify that the treatment is the only difference between groups and control for non-treatment effects such as frequency of contact.
- 4 Employing an intention to treat analysis to evaluate the effectiveness of CACR.

Systematic Review References

- Bark, M., Revheim, N., Huq, F., Kaldherov, V., Ganz, Z.V., & Medalia, A. (2003). The impact of cognitive remediation on psychiatric symptoms in schizophrenia. *Schizophrenia Research*, 63 (3), 229–235.
- Barch, D. M., & Keefe, R. S. E. (2010). Anticipating DSM-V: Opportunities and challenges for cognition and psychosis. *Schizophrenia Bulletin*, 36(1), 43-47.
- Bell, M. D., & Bryson, G. (2001). Work rehabilitation in schizophrenia: Does cognitive impairment limit improvement? *Schizophrenia Bulletin*, 27, 269-279.
- Bell, M., Fiszdon, J., Greig, T., Wexler, B., & Bryson, G. (2007). Neurocognitive enhancement therapy with work therapy in schizophrenia : 6-month follow-up of neuropsychological performance. *Journal of Rehabilitation Research and Development* 44, 761–770.
- Bell, M., Bryson, G., Greig, T., Fiszdon, J., & Wexler, B. E. (2005). Neurocognitive enhancement therapy with work therapy : Productivity outcomes at 6- and 12-month follow-ups. *Journal of Rehabilitation Research and Development*, 42, 829-838.
- Bellack, A.S., Dickinson, D., Morris, S.E., & Tenhula, W.N. (2005). The development of a computer-assisted cognitive remediation program for patients with schizophrenia. *The Israel Journal of Psychiatry and Related Sciences*, 42(1), 5-14.
- Bellucci, D. M., Glaberman, K., & Haslam, N. (2003). Computer-assisted cognitive rehabilitation reduces negative symptoms in the severely mentally ill. *Schizophrenia Research*, 59(2-3), 225-232.

- Benedict, R.H.B., Harris, A.E., Markow, T., McCormick, J.A., Nuechterlein, K.H., & Asarnow, R.F. (1994). Effects of attention training on information processing in schizophrenia. *Schizophrenia Bulletin* 20, 537–546.
- Bilder, R. M., Goldman, R. S., Robinson, D., Reiter, G., Bell, L., Bates, J. A. et al. (2000). Neuropsychology of first-episode schizophrenia: Initial characterization and clinical correlates. *American Journal of Psychiatry*, 157(4), 549-559.
- Burda, P.C., Starkey, T.W., Dominguez, F., & Vera, V. (1994). Computer-assisted cognitive rehabilitation of chronic psychiatric inpatients. *Computers in Human Behavior*, 10, 359–368.
- Cassidy, J.J., Easton, M., Capelli, C., Singer, A., & Bilodeau, A. (1996). Cognitive remediation of persons with severe and persistent mental illness. *Psychiatric Quarterly*, 67, 313– 321.
- Cavallaro, R., Anselmetti, S., Poletti, S., Bechi, M., Ermoli, E., Cocchi, F. et al. (2009). Computer-aided neurocognitive remediation as an enhancing strategy for schizophrenia rehabilitation. *Psychiatry Research*, 169(3), 191-196.
- Centre for Reviews and Dissemination. (2009). *Systematic reviews: CRD's guidance for undertaking reviews in health care*. The University of York: Retrieved 10 May 2012 from www.york.ac.uk/inst/crd/index_guidance.htm.
- d'Amato, T., Bation, R., Cochet, A., Jalenques, I., Galland, F., Giraud-Baro, E. et al. (2011). A randomized, controlled trial of computer-assisted cognitive remediation for schizophrenia. *Schizophrenia Research*, 125(2-3), 284-290.
- Dickinson, D., Tenhula, W., Morris, S., Brown, C., Peer, J., Spencer, K et al. (2010). A randomized, controlled trial of computer-assisted cognitive remediation for schizophrenia. *American Journal of Psychiatry*, 167(2), 170-180.

- Eack, S.M., Greenwald, D.P., Hogarty, S.S., Cooley, S.J., DiBarry, A.L., Montrose, D.M. et al. (2009). Cognitive enhancement therapy for early-course schizophrenia: Effects of a two-year randomized controlled trial. *Psychiatric Services, 60*(11), 1468-1476.
- Eack, S.M., Hogarty, G.E., Greenwald, D.P., Hogarty, S.S., & Keshavan, M.S. (2007). Cognitive enhancement therapy improves emotional intelligence in early course schizophrenia : preliminary effects. *Schizophrenia Research 89*, 308–311.
- Eaton, W.W., Thara, R., Federman, B., Melton, B., & Liang, K. (1995). Structure and course of positive and negative symptoms in schizophrenia. *Archives of General Psychiatry, 52* (2), 127-134.
- Fisher, M., Holland, C., Subramaniam, K., & Vinogradov, S. (2010). Neuroplasticity-based cognitive training in schizophrenia: An interim report on the effects 6 months later. *Schizophrenia Bulletin, 36*(4), 869-879.
- Fiszdon, J.M., Bryson, G.J., Wexler, B.E., & Bell, M.D. (2004). Durability of cognitive remediation training in schizophrenia: performance on two memory tasks at 6-month and 12-month follow-up. *Psychiatry Res, 125*, 1–7.
- Fiszdon J.M., Choi, J., Bryson, G.J., & Bell, M.D. (2006). Impact of intellectual status on response to cognitive task training in patients with schizophrenia. *Schizophrenia Research 87*, 261–269
- Galderisi, S., Piegari, G., Mucci, A., Acerra, A., Luciano, L., Rabasca, A. F. et al. (2010). Social skills and neurocognitive individualized training in schizophrenia: Comparison with structured leisure activities. *European Archives of Psychiatry and Clinical Neuroscience, 260*(4), 305-315.

- Gold, J. M. (2004). Cognitive deficits as treatment targets in schizophrenia. *Schizophrenia Research*, 72(1), 21-28.
- 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”? *Schizophrenia Bulletin*, 26(1), 119-136.
- Green, M. F. (1996). What are the functional consequences of neurocognitive deficits in schizophrenia? *The American Journal of Psychiatry*, 153(3), 321-330.
- Greig, T.C., Zito, W., Wexler, B.E., Fiszdon, J., & Bell, M.D. (2007). Improved cognitive function in schizophrenia after one year of cognitive training and vocational services. *Schizophrenia Research* 96, 156–161.
- Grynszpan, O., Perbal, S., Pelissolo, A., Fossati, P., Jouvent, R., Dubal, S. et al. (2011). Efficacy and specificity of computer-assisted cognitive remediation in schizophrenia: A meta-analytical study. *Psychological Medicine*, 41(01), 163-173.
- Heaton, R. K., Gladsjo, J. A., Palmer, B. W., Kuck, J., Marcotte, T. D., & Jeste, D. V. (2001). Stability and course of neuropsychological deficits in schizophrenia. *Archives of General Psychiatry*, 58, 24-32.
- Hermanutz, M., & Gestrich, J. (1991). Computer-assisted attention training in schizophrenics: A comparative study. *European Archives of Psychiatry and Clinical Neuroscience*, 240(4-5), 282-287.
- Heydebrand, G. (2007) Issues in Rehabilitation of Cognitive Deficits in Schizophrenia: A Critical Review. *Current Psychiatry Reviews*, 3 (3), 186-195.

- Hodge, M. A., Siciliano, D., Withey, P., Moss, B., Moore, G., Judd, G. et al. (2010).
A randomized controlled trial of cognitive remediation in schizophrenia.
Schizophrenia Bulletin, 36(2), 419-427.
- Hogarty, G. E., Flesher, S., Ulrich, R., Carter, M., Greenwald, D., Pogue-Geile, M. et al. (2004). Cognitive enhancement therapy for schizophrenia: Effects of a 2-year randomized trial on cognition and behavior. *Archives of General Psychiatry*, 61(9), 866-876.
- Hogarty, G.E, Greenwald, D.P., & Eack, S.M. (2006). Durability and Mechanism of Effects of Cognitive Enhancement Therapy. *Psychiatric Services*, 57 (12), 1751-1757.
- Hunter, R., & Barry, S. (2011). Negative symptoms and psychosocial functioning in schizophrenia: neglected but important targets for treatment. *European Psychiatry*, 27 (6), 432-436.
- Krabbendam, L., & Aleman, A. (2003). Cognitive rehabilitation in schizophrenia: A quantitative analysis of controlled studies. *Psychopharmacology*, 169, 376-382.
- Kurtz, M. M., Moberg, P. J., Gur, R. C., & Gur, R. E. (2001). Approaches to cognitive remediation of neuropsychological deficits in schizophrenia: A review and meta-analysis. *Neuropsychology Review*, 11(4), 197-210.
- 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? *Schizophrenia Research*, 89, 251–260.
- Kurtz, M.M., Seltzer, J.C., Fujimoto, M., Shagan, D.S., & Wexler, B.E. (2009). Predictors of change in life skills in schizophrenia after cognitive remediation. *Schizophrenia Research*, 107 (2-3), 267-274.

- Kurtz, M.M., Wexler, B.E., Fujimoto, M., Shagan, D.S., & Seltzer, J.C. (2008). Symptoms versus neurocognition as predictors of change in life skills in schizophrenia after outpatient rehabilitation. *Schizophrenia Research, 102* (1-3), 303-311.
- Lecardeur, L., Stip, E., Giguere, M., Blouin, G., Rodriguez, J.P., & Champagne Lavau, M. (2009). Effects of cognitive remediation therapies on psychotic symptoms and cognitive complaints in patients with schizophrenia and related disorders: a randomized study. *Schizophrenia Research, 111*(1-3):153-8.
- Lewis, L., Unkefer, E.P., O'Neal, S.K., Crith, C.J., & Fultz, J. (2003). Cognitive rehabilitation with patients having persistent, severe psychiatric disabilities. *Psychiatric Rehabilitation, 26*, 325–331.
- Lindenmayer, J., McGurk, S.R., Mueser, K.T., Khan, A., Wance, D., Hoffman, L., Wolfe, R. et al. (2008). A randomized controlled trial of cognitive remediation among inpatients with persistent mental illness. *Psychiatric Services, 59* (3), 241-247.
- López-Luengo, B., & Vázquez, C. (2003). Effects of Attention Process Training on cognitive functioning of schizophrenic patients. *Psychiatry Research, 119*(1-2), 41-53.
- Mangalore, R., & Knapp, M. (2007). Cost of schizophrenia in England. *The Journal of Mental Health Policy and Economics, 10*(1), 23-41.
- McGurk, S. R., Mueser, K. T., DeRosa, T. J., & Wolfe, R. (2009). Work, recovery, and comorbidity in schizophrenia: A randomized controlled trial of cognitive remediation. *Schizophrenia Bulletin, 35*(2), 319-335.

- McGurk, S. R., Twamley, E. W., Sitzer, D. I., McHugo, G. J., & Mueser, K. T. (2007). A meta-analysis of cognitive remediation in schizophrenia. *American Journal of Psychiatry*, *164*(12), 1791-1802.
- Medalia, A., Aluma, M., Tryon, W., & Merriam, A. E. (1998). Effectiveness of attention training in schizophrenia. *Schizophrenia Bulletin*, *24*(1), 147-152.
- Medalia, A., Choi, J., 2009. Cognitive remediation in schizophrenia. *Neuropsychology Review*, *19* (3), 353–364.
- Medalia, A., Revheim, N., & Casey, M. (2000). Remediation of memory disorders in schizophrenia. *Psychological Medicine* *30*, 1451–1459.
- Medalia, A., Revheim, N., & Casey, M. (2001). The remediation of problem-solving skills in schizophrenia. *Schizophrenia Bulletin* *27*, 259–267.
- Medalia, A., Revheim, N., & Casey, M. (2002). Remediation of problem-solving skills in schizophrenia: evidence of a persistent effect. *Schizophrenia Research* *57*, 165–171.
- Medalia, A., Revheim, N., & Herlands, T. (2009). *Cognitive remediation for psychological disorders: Therapist guide (treatments that work)*. USA: Oxford University Press.
- Mohamed, S., Rosenheck, R., & Swartz, M. (2008). Relationship of cognition and psychopathology to functional impairment in schizophrenia. *American Journal of Psychiatry*, *165*, 978-987.
- Morris, S. (2008). Estimating effect sizes from pretest-posttest-control group designs. *Organizational Research Methods*, *11*(2), 364-386.

- 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. *Schizophrenia Research*, 72(1), 29-39.
- Olbrich, R., & Mussgay, L. (1990). Reduction of schizophrenic deficits by cognitive training: an evaluative study. *European Archives of Psychiatry and Neurological Sciences*, 239, 366–369.
- Pilling, S., Bebbington, P., Kuipers, E., Garety, P., Geddes, J., Martindale, B. et al. (2002). Psychological treatments in schizophrenia: II. meta-analyses of randomized controlled trials of social skills training and cognitive remediation. *Psychological Medicine*, 32, 783-791.
- Rauchensteiner, S., Kawohl, W., Ozgurdal, S., Littmann, E., Gudlowski, Y., Witthaus, H. et al. (2011). Test-performance after cognitive training in persons at risk mental state of schizophrenia and patients with schizophrenia. *Psychiatry Research*, 185 (3), 334-339.
- Roder, V., Mueller, D.R., Mueser, K.T., & Brenner, H.D. (2006). Integrated psychological therapy (IPT) for schizophrenia: is it effective? *Schizophrenia Bulletin*, 32 (Suppl. 1), S81–S93.
- Sartory, G., Zorn, C., Groetzinger, G., & Windgassen, K. (2005). Computerized cognitive remediation improves verbal learning and processing speed in schizophrenia. *Schizophrenia Research*, 75, 219–223.
- Scottish Intercollegiate Guidelines Network (SIGN) guideline. (2009). *Schizophrenia: Core interventions in the treatment and management of schizophrenia in adults in primary and secondary care*. Edinburgh, UK.
- Spaulding, W.D., Fleming, S.K., Reed, D., Sullivan, M., Storzbach, D., & Lam, M.

- (1999). Cognitive functioning in schizophrenia: Implications for psychiatric rehabilitation. *Schizophrenia Bulletin*, 25(2), 275-289.
- Surti, T.S., Corbera, S., Bell, M.D., & Wexler, B.E. (2011). Successful computer-based visual training specifically predicts visual memory enhancement over verbal memory improvement in schizophrenia. *Schizophrenia Research*, 132(2-3), 131-134.
- Twamley, E. W., Doshi, R. R., Nayak, G. V., Palmer, B.W., Golshan, S., Heaton, R.K. et al. (2002). Generalized cognitive impairments, ability to perform everyday tasks, and level of independence in community living situations of older patients with psychosis. *American Journal of Psychiatry*, 159(12), 2013-2020.
- Twamley, E.W., Jeste, D.V., & Bellack, A.S. (2003). A review of cognitive training in schizophrenia. *Schizophrenia Bulletin*, 29(2), 359-382.
- Vesterager, L. Christensen, T. Olsen, B.B., Krarup, G., Forchhammer, H., & Melau, M. (2011). Cognitive training plus a comprehensive psychosocial programme (OPUS) versus the comprehensive psychosocial programme alone for patients with first-episode schizophrenia (the NEUROCOM trial): A study protocol for a centrally randomised, observer-blinded multi-centre clinical trial. *Trials*, 12, 35-
- Vauth, R., Corrigan, P. W., Clauss, M., Dietl, M., Dreher-Rudolph, M., Stieglitz, R. et al. (2005). Cognitive strategies versus self-management skills as adjunct to vocational rehabilitation. *Schizophrenia Bulletin*, 31(1), 55-66.
- Vita, A., De Peri, L., Barlati, S., Cacciani, P., Deste, G., Poli, R. et al. (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. *Schizophrenia Research, 133*(1-3), 223-231.

Wolwer, W., Frommann, N., Halfmann, S., Piaszek, A., Streit, M., & Gaebel, W. (2005). Remediation of impairments in facial affect recognition in schizophrenia: Efficacy and specificity of a new training program. *Schizophrenia Research, 80*(2-3), 295-303.

World Health Organisation (2012) *Mental health: Schizophrenia*. Available at: http://www.who.int/mental_health/management/schizophrenia/en/. Retrieved 4 June 2012.

Wykes, T., & Spaulding, W. D. (2011). Thinking about the future cognitive remediation therapy. What works and could we do better? *Schizophrenia Bulletin, 37*(suppl 2), S80-S90.

CHAPTER 2: INTRODUCTION

2.1 Effects of CACR on cognitive functioning

To date, only one review has evaluated the effects of CACR on cognitive functioning in individuals with a diagnosis of either schizophrenia or schizoaffective disorder.

Grynszpan *et al.* (2011) found results in line with previous reviews of cognitive remediation reviews, and reported that CACR had an effect size of 0.38 on general cognition. Although this meta-analysis, of sixteen randomised controlled trials provided substantial evidence supporting the efficacy of CACR, a number of negative reports have also been published. Murthy *et al.* (2012) investigated the effects of CACR on cognitive functioning and functional capacity in individuals with schizophrenia, in a multi-site clinical trial involving fifty-five participants. Murthy *et al.* (2012) found that participants improved on the training tasks but this effect did not generalise to independent measures of cognitive functioning or functional capacity. This study used a CACR intervention that aimed to train only auditory information processing; this limitation may account for the lack of findings.

Dickinson *et al.* (2010) also conducted a randomised controlled trial investigating the benefits of cognitive remediation on cognitive functioning and functional outcome in schizophrenia. Similar to Murthy *et al.* (2012), this study found participants' performance improved on the training tasks, but these improvements did not generalise to performance on neuropsychological tests or assessments of psychosocial functioning. Dickinson *et al.* (2010) developed a cognitive remediation programme to use in their study, and may have benefited from using a programme

that had been used in previous research and had an established evidence base. These reports of negative results highlight the need for further investigations into the key components of successful cognitive remediation to inform future treatments.

Studies investigating the effects of CACR vary in the software used, the tasks completed, and the duration or intensity of the intervention. One component that is of particular interest is the minimum dose of intervention required to improve cognitive functioning. Field (1997) reported that a three week intervention consisting of two sessions per week was not effective at significantly improving attention in individuals with a diagnosis of schizophrenia.

However, Hermanutz & Gestrich (1991) reported that a four week CACR intervention that consisted of four sessions per week was effective at improving attention in individuals with a diagnosis of schizophrenia, but did not improve ratings of social, occupational and psychological functioning as assessed by the Global Assessment Scale (GAS). Similarly, Medalia, Revheim & Casey (2001) reported that a five week intervention, consisting of two sessions per week, significantly improved problem solving skills in individuals with a diagnosis of schizophrenia. Further evidence in support of a brief CACR intervention was provided by Bellucci *et al.* (2002) who found that an eight week CACR intervention consisting of two sessions per week significantly improved verbal memory and attention in individuals with schizophrenia.

The mixed results from studies investigating the benefits of CACR, suggest that further research is needed to evaluate the efficacy of brief CACR interventions. The studies that have previously investigated brief CACR interventions have a number of weaknesses. More specifically, only one of the studies discussed above investigated whether any effects of CACR generalised to psychosocial functioning, despite this being one of the main goals of CACR. Additionally, these studies did not include any form of follow-up to investigate whether the effects of a brief CACR intervention were sustained.

2.2 Effects of CACR on psychosocial functioning

Although there is growing evidence that CACR is effective at improving cognitive functioning in individuals with schizophrenia, there are mixed results regarding whether these benefits generalise to psychosocial functioning.

Hogarty (2004) compared the effects of cognitive enhancement therapy with enriched supportive therapy, on cognitive functioning and behavioural outcome measures. This study found that cognitive enhancement therapy had a greater effect than enriched supportive therapy on social adjustment, at both the 12 and 24-month follow-up periods. This study indicates that the effects of CACR may generalise to social functioning in patients with a diagnosis of schizophrenia and that these effects are durable and last for up to 2-years post-intervention. A further study conducted by Vita *et al.* (2010), which employed an RCT design involving seventy-two participants, found that CACR had a significant effect on different aspects of

psychosocial functioning as assessed by the Health of the Nation Outcome Scale (HoNOS).

Cavallaro *et al.* (2009) evaluated a three month cognitive remediation intervention in addition to a standard rehabilitation programme, and reported that patients in the CACR group had better outcomes as assessed by the Quality of Life Scale (QLS). This study provided encouraging results that CACR can have a positive impact on psychosocial functioning, as well as improving cognitive functioning.

In addition to the above research, Poletti *et al.* (2010) reported that using CACR, in addition to a standard rehabilitation treatment, had a significant effect over placebo training and standard rehabilitation treatment, on quality of life at post- intervention. Interestingly, the improvement was seen to increase progressively at the 6 and 12-month follow-up in the experimental group, suggesting that the effect continued to increase over time after the intervention had been stopped (Poletti *et al.*, 2010).

In addition to the encouraging results on quality of life, a growing number of articles have investigated the benefits of CACR on vocational outcome measures such as employment status, hours worked and money earned (Bell *et al.*, 2005; Bell *et al.*, 2008; Vauth *et al.*, 2005; McGurk *et al.*, 2009). A study investigating the benefits of CACR, (Bell *et al.*, 2005; Bell *et al.*, 2008) found that individuals who received neurocognitive enhancement therapy and work therapy, worked more hours and received better rates of pay than those who received work therapy alone, at both 6 and 12-month follow-up. Lindenmayer *et al.* (2008) also reported that individuals

who received 24-hours of CACR, worked more weeks than a computerised control group over the 12-month follow-up period.

Similar findings were reported by Vauth *et al.* (2005) who found that individuals who received CACR plus vocational rehabilitation, were more likely to be in a job placement at 12-month follow-up than those who received training for the self management of negative symptoms and vocational rehabilitation, or vocational rehabilitation alone. Further analyses of the results of this study identified that improvement in verbal memory was a greater predictor of successful job placement than pre-treatment history of employment (Vauth *et al.*, 2005). This study identified that verbal memory may be a key target for vocational interventions aiming to improve functioning in employment.

Further research into the benefits of CACR on vocational outcome measures was conducted by McGurk *et al.* (2009) who reported better work outcomes over the 2 year follow-up period for individuals who received CACR and vocational rehabilitation than those who received vocational rehabilitation alone. Research into the use of CACR alongside vocational rehabilitation suggests that CACR has a positive effect when used in combination with other forms of rehabilitation seeking to improve occupational functioning.

Despite a growing number of papers reporting that CACR has a positive effect on various measures of psychosocial functioning, a number of papers have also provided negative results. d'Amato *et al.* (2010) investigated the benefits of CACR

in addition to standard treatment in individuals with a diagnosis of schizophrenia.

d'Amato *et al.* (2010) reported that CACR had significant effects on a number of cognitive functions but no effect on measures of social autonomy or quality of life.

An additional study conducted by Hermanutz & Gestrich (1991) evaluated the effects of CACR on clinicians' ratings of social, occupational and psychological functioning as assessed by the Global Assessment Scale (GAS). This study found no significant difference between groups on overall GAS scores across time, suggesting that CACR did not improve functioning as assessed by The GAS.

2.3 Rationale for the current research

The literature investigating the effects of CACR on cognitive functioning and psychosocial functioning has produced mixed results and there is a need for further research in this field to expand the existing evidence base. Previous research investigating the effects of brief CACR interventions has produced both positive and negative results; therefore, there is a need for brief CACR intervention studies that investigate whether any effects of CACR on cognitive functioning are maintained across time and whether effects generalise to psychosocial functioning.

A recent report from the Working Group Conference on Multi-Site Trial Design for Cognitive Remediation in Schizophrenia (Keefe *et al.*, 2011) highlighted that psychosocial functioning is influenced by a number of factors and that a measure of functional capacity, such as the University of California in San Diego Performance-Based Skills Assessment-Brief (Patterson *et al.*, 2001) should be included in studies investigating the benefits of cognitive remediation.

Clinically, it is of great interest to investigate whether a brief CACR intervention can improve cognitive functioning and psychosocial functioning in patients with a diagnosis of schizophrenia.

2.4 Aims/Hypotheses

2.4.1 Aims

The aim of the current thesis is to conduct an experimental study to investigate the effects of a brief CACR intervention on cognitive functioning, functional capacity and everyday social functioning in individuals with a diagnosis of schizophrenia or schizoaffective disorder. The research was considered to add to the previous literature by using a superior measure of cognitive functioning recommended for use in clinical trials. Recent recommendations also highlight the need for cognitive remediation research to include a measure of functional capacity. The current study included a recommended measure of functional capacity to investigate any effects of CACR. Finally, the notable deficits in social functioning observed in this population resulted in a measure of social functioning being included to explore any potential effects of CACR on everyday social functioning.

2.4.2 Hypotheses

After reviewing the selected literature the following hypotheses were proposed:

1. A five week CACR intervention, consisting of two sessions per week, will improve cognitive functioning as assessed by the NIMH Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery (MCCB).
2. A five week CACR intervention, consisting of two sessions per week, will improve functional capacity as measured by the University of California in San Diego (UCSD) Performance Based Skills Assessment-brief (UPSA-brief).
3. A five week CACR intervention, consisting of two sessions per week, will improve social functioning as measured by three subtests of the Social Functioning Scale (SFS).

CHAPTER 3: METHODOLOGY

3.1 Design

The study employed a repeated measures within-subjects design, with participants acting as their own controls. In order to investigate the effects of a computer-assisted cognitive remediation (CACR) intervention on cognitive functioning, functional capacity and everyday social functioning, participants completed the outcome measures at four time points throughout the study. The baseline assessment and the pre-intervention assessment served as the control for the current study. All participants were followed up one-month post-intervention to investigate the durability of any observed gains. Variables measured included cognitive functioning across seven cognitive domains, functional capacity and social functioning.

3.2 Power Analysis

G*Power version 3 is a power analysis programme for statistical tests commonly used in social and behavioural research (Faul, Erdfelder & Buchner, 2007). The sample size for the current project was determined through a-priori power calculation using G*Power version 3. A review of the previous literature was conducted to establish an appropriate effect size that could be used to determine the required sample size for the current study. McGurk *et al.* (2007) conducted a meta-analysis of the effects of cognitive remediation on cognitive functioning, symptoms and psychosocial functioning and reported effect sizes in the medium range for overall cognitive functioning (0.41). Additionally, Grynszpan *et al.* (2010) reported that CACR enhanced general cognition with a mean effect size of 0.38. With these effect

sizes in mind, a sample size of twenty-four participants was determined for the current study through the use of the following input parameters detailed in Table 3.1.

Table 3.1: G* Power 3 Output from A Priori Sample Size Calculation

ANOVA: Repeated measures within factors		
Input	Effect size f	0.25
	Alpha error prob	0.05
	Power	0.8
	Number of groups	1
	Number of measurements	4
	Corr among rep measures	0.5
	Nonsphericity correction	1
	Output	Noncentrality parameter
	Critical F	2.7375
	Numerator df	3
	Denominator df	69
	Total sample size	24
	Actual power	0.8168

Previous studies using the same cognitive remediation software package had reported attrition rates varying between 9 per cent (McGurk *et al.*, 2005) and 14 per cent (Cavallaro *et al.*, 2009). The project aimed to recruit a minimum of thirty-two participants to allow for a 25 per cent dropout rate to ensure the required numbers of participants completed the study to warrant adequate power for analyses.

3.3 Participants

Adult participants aged between 25 and 60 (mean age of 49.9) with a psychiatric diagnosis of schizophrenia or schizoaffective disorder as classified by the ICD10, were recruited for the study through the Psychiatric Rehabilitation and Adult Mental Health services within NHS Grampian. The current study employed the following inclusion/exclusion criteria:

3.3.1 Inclusion

- Participants had to be adults (aged 18 to 64) with a diagnosis of schizophrenia or schizoaffective disorder as classified by the ICD10.
- Participants had to be in current contact with services in NHS Grampian
- Participants had to be willing and able to commit to the full intervention
- Participants had to be literate in English language and able to follow on screen instructions.

3.3.2 Exclusion

- Participants were excluded if they were acutely unwell.
- Participants were excluded if they were involved in other research projects within NHS Grampian.

3.4 Procedure

Initially, an email was sent to consultant psychiatrists working in Psychiatric Rehabilitation and Adult Mental Health services within NHS Grampian, requesting permission to attend MDT meetings, to discuss the project and to identify potential participants. The researcher (J.M) then attended MDT meetings to meet with healthcare professionals, give an overview of the study, answer questions and ascertain whether there were any potential participants under the care of each team.

Healthcare professionals then gave patients who met the inclusion criteria, and had capacity to consent, an invitation letter (appendix 4) and an information sheet (appendix 5) outlining the project. Some teams opted to send out the information

packs to suitable patients, with capacity to consent, rather than giving them out during routine appointments. Interested patients were asked to contact the researcher directly, alternatively they gave their permission for their contact details to be passed onto the researcher and the researcher contacted them directly, following a waiting period of at least 24 hours.

Any individuals who were interested in participating were invited to meet with the researcher for an initial appointment. During this meeting, the information sheet was discussed and potential participants were given the opportunity to briefly engage with the CACR intervention in order to gain additional insight into the requirements of the study. All participants were informed that they would be required to meet the researcher twice a week, for a five week period, to participate in the intervention. Additionally, they were informed that they would complete four assessments over the course of the research using the standardised outcome measures. When individuals indicated they were interested in taking part in the research project, the consent form (appendix 6) was discussed and informed consent was obtained. Participants were given the opportunity to ask questions and were informed that their participation was voluntary and they could withdraw from the study at any time. After informed consent was obtained, a letter (appendix 7) was sent to participants' GPs informing them of the research project and their patients' participation.

An appointment was scheduled for the baseline assessment, during which participants completed a cognitive assessment using the National Institute for Mental Health's (NIMH) Measurement and Treatment Research to Improve Cognition in

Schizophrenia (MATRICS) Consensus Cognitive Battery (MCCB), an assessment of functional capacity using the University of California in San Diego (UCSD) performance based skills assessment-brief (UPSA-brief) and an assessment of social functioning using three subtests of the Social Functioning Scale (SFS).

Demographic information was also collected directly from participants at this stage.

Following a four week control waiting period, the pre-intervention assessment was then completed and the participants started the CACR intervention (Cogpack professional version 8.34). The intervention was run by the researcher or a support worker, either individually or in groups of up to three participants. During the intervention, participants met with the researcher or support worker for up to 50 minutes, twice a week, for a five week period. All participants were offered a total of ten sessions of CACR and were encouraged to complete at least five hours of the intervention. Some patients had difficulty concentrating for 50 minutes and in such cases shorter sessions were offered to accommodate individual needs. If participants completed less than five hours of CACR after attending ten appointments, they were offered additional appointments until the minimum of five hours had been completed. Where possible, participants were offered the opportunity of further appointments, to account for any missed appointments during the research project. During their attendance, participants engaged with the CACR intervention and completed tasks designed to train the cognitive deficits frequently found in individuals with a diagnosis of schizophrenia. All participants were informed they could take breaks as required during the intervention.

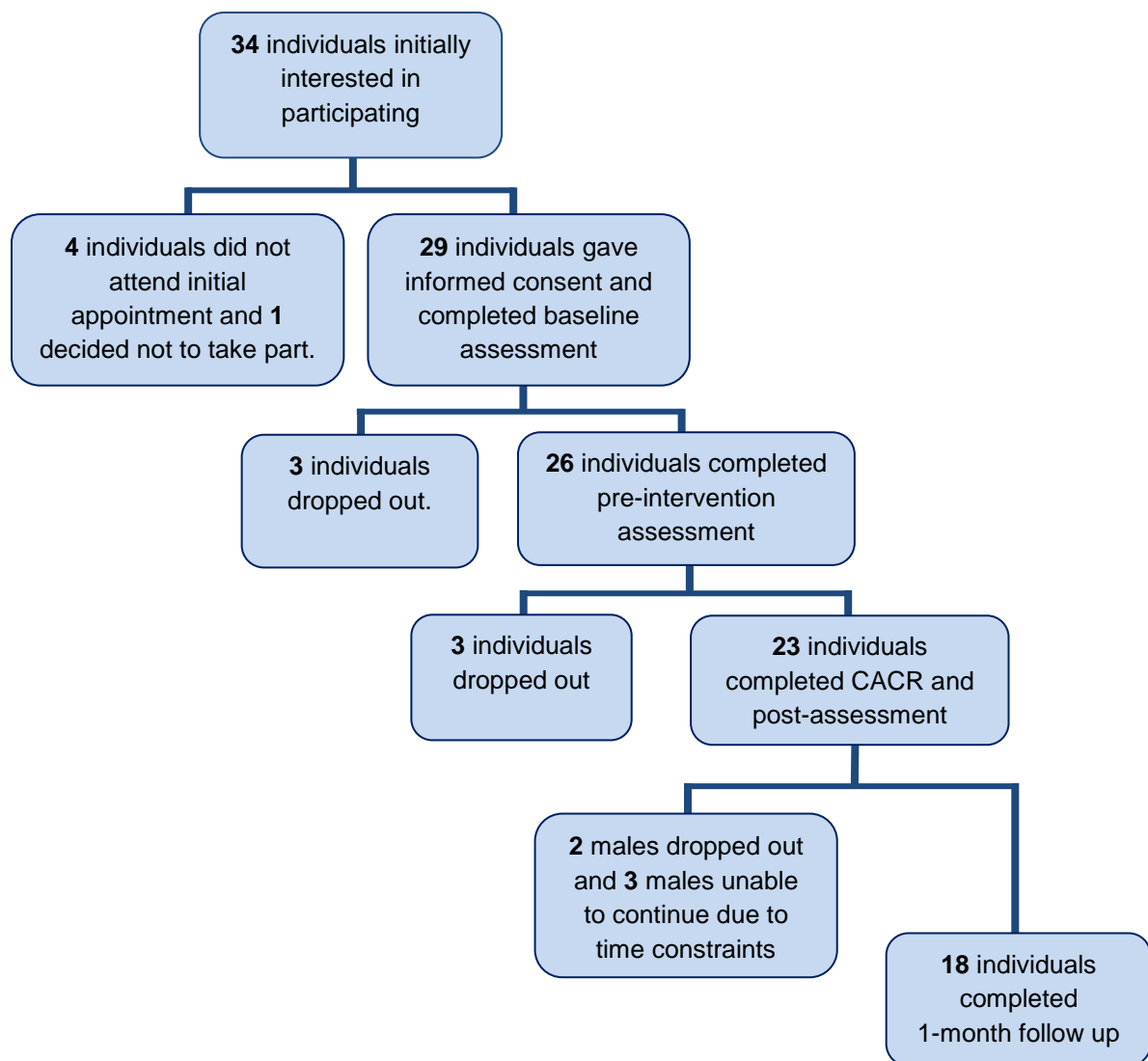
After the intervention period, participants completed the post-intervention assessment and were then invited back for a follow-up assessment, one-month after completing the intervention. During the one-month follow-up all participants were offered the opportunity to receive individual feedback on their performance during their assessment.

3.5 Recruitment

Initially 34 individuals expressed an interest in taking part, however, only 29 individuals (85 per cent) went on to give informed consent to participate in the study. Three participants dropped out after completing the first assessment (two experienced a deterioration in mental health and one could not commit enough time to complete the project). A further three participants dropped out after completing the second assessment (one experienced a deterioration in mental health and two could not commit enough time to complete the project). Two participants dropped out after completing the post-intervention assessment. In summary, a total of twenty-nine participants completed the initial assessment. Of these, twenty-six completed the pre-intervention assessment and twenty-three completed both the CACR intervention and the post-intervention assessment. At the time of analysis, eighteen participants had completed the one-month follow-up assessment.

Throughout the study, contact was maintained with the consultant psychiatrists responsible for the participants' care, to monitor the participants' ongoing mental state and eligibility to take part in the study. The recruitment process and number of participants completing each assessment can be seen in Figure 3.1.

Figure 3.1: Flow chart detailing the recruitment process and dropout rate



3.6 Ethical considerations

3.6.1 Ethical approval

The methodology of the current study was reviewed by the University of Edinburgh. In addition, a formal application for ethical approval was submitted to the North of Scotland Research ethics Service (NRES) using the Integrated Research Application System for ethical applications. Ethical approval for the project was granted and

confirmed in writing on the 2nd September 2011 (appendix 8). Approval from the local Research and Development department was also granted and confirmed by letter on the 26th September 2011 (appendix 9).

3.6.2 Informed consent and confidentiality

Informed consent was obtained from all participants prior to their participation in the research. The clinical team/referrer of each potential participant assessed capacity to consent, prior to giving potential participants information about the research project. During the initial appointment with the researcher, the nature of the study was explained to all potential participants. After reading the invitation letter (appendix 4) and participant information sheet (appendix 5), all participants provided signed informed consent (appendix 6) to confirm that they understood the nature of the study prior to their participation. Each participant was given a copy of their signed consent form to keep and an additional copy was filed in their medical notes.

Individuals were informed that participation was voluntary and they were free to withdraw from the study at any time. It was also emphasised to participants that withdrawal from the study would not impact their ongoing care from NHS Grampian. Finally, participants were informed that all data collected during the study would remain confidential and would not be shared with any healthcare professionals involved in their care.

3.6.3 Risks to participants

There were minimal risks to participants identified during the course of the current study. It was acknowledged that the intervention was a substantial time commitment for participants; therefore, refreshments were made available during the study. Additionally, participants were informed that they could take breaks as required during the intervention period and were offered shorter appointments if the 50 minute appointment was deemed to be too long. The researcher, where possible, offered to reschedule any appointments missed or cancelled by participants.

3.7 Measures

3.7.1 Demographic and clinical information

Demographic and clinical information was collected from participants during the initial appointment. In some cases, with permission, additional information regarding their diagnosis was obtained from the participants' psychiatrists.

Information obtained during the current study included:

- Diagnosis
- Date of birth/age
- Gender
- Inpatient/outpatient status
- Current medication

3.7.2 Cognitive Functioning

MATRICS consensus cognitive battery (Nuechterlein & Green, 2006).

Although a number of studies have examined cognitive enhancing interventions in individuals with schizophrenia, the lack of a consensus cognitive battery for measuring changes in cognitive functioning has been a major obstacle in the comparison and evaluation of such interventions. The NIMH Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) initiative developed a consensus cognitive battery that can be used to measure changes in cognitive functioning and evaluate cognitive enhancing interventions (Nuechterlein & Green, 2006). Initially, the MATRICS initiative evaluated previous research to identify a common set of cognitive impairments in individuals with a diagnosis of schizophrenia. This process identified seven separate cognitive domains that were found to be frequently impaired: speed of processing, attention/vigilance, working memory, verbal learning and memory, visual learning and memory, reasoning and problem solving and social cognition (Nuechterlein, Barch, Gold, Goldberg, Green & Heaton, 2004).

This initial process led to the structured development of the MATRICS consensus cognitive battery (MCCB), which involved the evaluation of over 90 assessments, across the seven cognitive domains. The final test battery selection was based on specific criteria relating to test-retest reliability, utility as a repeated measure, relationship to functional status, sensitivity in response to pharmacological agents and practicality for clinical trials and tolerability for patients (Nuechterlein *et al.*, 2008). All of the assessments included in the final battery have at least acceptable test-retest reliability (above .70) and three of the subtests have alternate forms to

minimise practice affects (Nuechterlein *et al.*, 2008). The standardised battery was co-normed on a sample of 300 community-based individuals stratified by age, which allows for the comparison of scores using a common metric, something that has proved difficult in previous research.

The MCCB has been utilised by a number of drug trials, and is recommended for use in clinical trials of cognitive remediation as a valid and sensitive measure of cognitive impairment in schizophrenia that is related to functional outcome (August *et al.*, 2011).

For the current study, the structured consideration of psychometric properties in the development of the battery resulted in the MCCB being the most suitable measure. Previous cognitive remediation studies have utilised multiple tests, with individual norms. A clear advantage of using the MCCB is that the measure was co-normed on one sample, making it easier to draw comparisons between studies that utilise the MCCB. It is envisaged that future cognitive remediation and pharmacological intervention studies will employ this measure and therefore allow direct comparisons to be drawn between the effects of various interventions. The MCCB was specifically developed to measure change in trials of cognition enhancing interventions and it is considered to be the gold standard for measuring cognition in schizophrenia in clinical trials (Keefe, 2011), hence it was selected for use in the current research.

3.7.3 Functional Capacity

The University of California in San Diego (UCSD) Performance Based Skills Assessment- brief (Patterson *et al.*, 2001).

Attempts to assess functioning in patients with a severe mental illness have previously involved the use of self-report measures, proxy rated measures, clinician rated measures and direct observations of behaviour. Patterson *et al.* (2001) discussed the merits of each technique and highlighted that self-report measures may be influenced by clinical symptoms, that reliable proxy raters are not available for many individuals with severe mental illness and that clinician ratings are often based on only a brief clinical appointment with the individual. In light of these weaknesses, Patterson *et al.* (2001) argued that performance-based measures of functional capacity offer a reliable and valid measure of functioning, free from some of the difficulties associated with alternative measures of functioning. Performance-based measures of functional capacity to perform everyday living skills are becoming more widely used as outcome measures in research involving individuals with severe mental illness (Patterson *et al.*, 2006; Granholm *et al.*, 2005; Dickenson *et al.*, 2010; Murthy *et al.*, 2012).

One advantage of employing measures of functional capacity, which assesses an individual's capacity to perform everyday activities, is that such measures are free from environmental and social factors that may impact on everyday functioning, and therefore provide a direct assessment of an individual's functioning. The popularity of functional capacity measures has increased in recent times and there is a growing

body of literature supporting the use of such measures in research (Mausbach *et al.*, 2009).

The University of California in San Diego (UCSD) Performance Based Skills Assessment (UPSA) was developed to assess basic living skills in community-based individuals with schizophrenia, across the following five domains: Financial Skills, Communication, Organisation/Planning, Transportation and Household Management. Scores for each subtest are transformed into a 0 to 10 scale to allow for comparison and then multiplied by 2 to give a total score out of 100, with higher scores reflecting higher functional capacity (Patterson *et al.*, 2001). Patterson *et al.* (2001) reported excellent inter-rater reliability (0.91) although it should be noted that this figure was only based on a subsample of twenty individuals. Patterson *et al.* (2001) also reported significant correlations between UPSA scores and cognitive impairment and severity of negative symptoms. Although Patterson *et al.* (2001) recommended the UPSA as a useful tool for assessing functional capacity in adults with severe mental illness, the findings were based on a relatively small sample size (50 individuals with a diagnosis of schizophrenia and 20 healthy controls).

Despite this criticism, a number of studies have since provided further evidence for the utility of this measure. Mausbach *et al.* (2007) found evidence to support the sensitivity of this measure to predict living status, suggesting a cut-off score of 75 or 80 as a predictor of independent living status. In addition to this, it has been demonstrated that the UPSA correlates with cognitive functioning as measured using the MCCB, $r=.61$ (Green *et al.*, 2008) and the Brief Assessment of Cognition in

Schizophrenia (BACS), $r=.65$ (Keefe *et al.*, 2006). Additionally, the UPSA was rated favourably in terms of tolerability by participants undergoing assessment (Green *et al.*, 2008), suggesting that the measure is well received.

The UPSA-brief is a shorter version of the UPSA, which consists of two of the five original subscales: financial and communication skills. Each of the two subscales gives a maximum score of 50 points, which are combined to give a total score ranging from 0 to 100 points, with higher scores reflecting higher levels of functional capacity. Mausbach *et al.* (2007) found that the UPSA-brief total score was significantly correlated ($r =.93$) with the five-subscale UPSA; in addition, the UPSA-brief and the UPSA did not differ significantly in their usefulness for predicting residential status, although the recommended cut-off for the UPSA-brief is 60.

The test-retest reliability of the UPSA was investigated by Leifker *et al.* (2010) who found that the UPSA-brief reliabilities ranged from $r =.66$ to $r =.81$ for periods of up to 36 months. Leifker *et al.* (2010) reported practice effects for the UPSA-brief ranging from 0.01 to 0.16 for periods up of up to 36 months, with the greatest effect size found over a 6-month period. The challenge of practice effects was considered in the present study due to the short time frame between each assessment; however, it was noted that assessment measures are not without weaknesses and the additional advantages of the UPSA-brief resulted in it being included in the present study.

Leifker *et al.* (2010) identified that relatively large changes in raw scores (21.32, SD 1.06) would be required between assessments to exceed a 90 per cent confidence

interval; this finding provided clear guidance for the interpretation of scores in the current study.

The UPSA-brief was selected for use in the current study, as it was recommended by the MATRICS working group conference on multi-site trials of cognitive remediation as an adequate short form measure of functional capacity (Keefe *et al.*, 2010), and it can be completed and scored in less than 10 minutes. Permission was obtained from the author to use the UPSA-brief in the current study. Approved adaptations were carried out, in line with previous adaptations for a European version, to localise the measure for use with a Scottish population (for example using British pounds instead of American dollars in the finance subtest).

3.7.4 Social functioning

The Social Functioning Scale (Birchwood *et al.*, 1990).

It has been argued that impairment of social functioning may reflect a primary impairment in schizophrenia (Bellack *et al.*, 1990). The assessment of social functioning is therefore an important factor in ongoing treatment research. The Social Functioning Scale (SFS) was developed to assess seven domains of functioning that are considered necessary for community functioning (Birchwood *et al.*, 1990). Items are scored on a four point scale, with higher scores reflecting a higher level of functioning. The raw scores of the seven domains are converted into a scaled score with a mean of 100 and SD of 15.

In a study involving 334 outpatients with a diagnosis of schizophrenia, and 100 control subjects, Birchwood *et al.* (1990) reported high internal reliability (alpha of 0.80) and inter-rater reliability (0.94). Although this provides clear support for the utility of this measure, the inter-rater reliability was derived from a small sub sample of only 30.

Although the SFS has reasonable psychometric properties, it was designed for use with community-based patients; therefore, its suitability for use with inpatients may be questionable. Despite this criticism, the SFS has become a well utilised measure for research purposes to assess social functioning in individuals with severe mental illness. A recent project funded by the National Institute of Mental Health, which aimed to enhance the measurement of real world outcomes through the evaluation of functioning measures, asked forty-eight experts to nominate scales that they believed best measured real world functioning. This process resulted in 59 measures being identified, which were then reviewed by a panel and rated on a 9-point scale (1=poor, 9=superb). The SFS was rated as one of the superior measures and was selected for the next stage of the research, which involves a validation study that is currently ongoing (Leifker *et al.*, 2011).

Previous research has demonstrated that scores on the SFS are significantly correlated with neuropsychological test performance (Dickerson *et al.*, 1996). Such findings indicate that cognitive enhancing treatments may lead to improvements in social functioning in individuals with a diagnosis of schizophrenia.

The SFS was selected for use in the current study as it was free for use in research, it demonstrated good psychometric properties, the reference period for the scale was unspecified and each domain was given a scaled score, meaning that a shorter version of the SFS could be administered in the current study. The SFS was obtained from the primary author, along with permission for use in the current research. The current study made use of three subtests: withdrawal/social engagement, independence performance and independence competence. The subscales that assessed functional capacity and functional performance were selected in order to keep in line with the distinction between functional capacity and functional performance.

3.8 Intervention

Cogpack professional software (version 8.34) is a computerised cognitive remediation package that was developed in Germany in 1985 and has been tested clinically throughout Europe in psychiatric populations since 1986. The current version used in the study consisted of 64 programmes that can be used to train various cognitive skills including: visuomotor, comprehension, reaction, vigilance, memory, language, intellectual and professional skills (Marker, 2011). Cogpack gives detailed instructions on-screen prior to starting tasks, and gives the opportunity of practice trials before starting the training series.

3.8.1 Selection of Cogpack for current study

There is growing literature supporting the use of Cogpack with patients with a diagnosis of schizophrenia. A number of studies have reported that using Cogpack

can significantly improve cognitive functioning (McGurk *et al.*, 2005; Cavallero *et al.*, 2009; Sartory *et al.*, 2005; Vaugh *et al.*, 2005; Wolwer *et al.*, 2005; Lindenmayor *et al.*, 2008) and daily functioning (McGurk *et al.*, 2005; Cavallero *et al.*, 2009, Poletti *et al.*, 2010) in this population.

Additionally, Bender *et al.* (2004) investigated the subjective experience of using Cogpack in 64 patients with schizophrenia, and reported that the CACR training was rated as highly acceptable by participants and experienced as very effective. In addition to this, following the training, self reported computer anxiety scores decreased, while subjective well-being scores significantly increased (Bender *et al.*, 2004). The above findings highlight that Cogpack is well received by individuals and there was a reasonable evidence base supporting the decision to select Cogpack for use in the current study.

3.8.2 Training series in current study

A previous meta-analysis was used as guidance when deciding the lengths and number of sessions offered in the current study. McGurk *et al.* (2007) demonstrated that the number of hours of cognitive remediation was not associated with the degree of improvement in cognitive functioning and therefore between five and fifteen hours of cognitive remediation were sufficient to produce changes in cognitive functioning. A further meta-analysis investigating the effects of CACR also reported that treatment duration and weekly frequency did not correlate significantly with effect size estimates (Grynszpan *et al.*, 2011). With this in mind, the current study aimed to

offer a brief, intensive intervention of a minimum of 5 hours of CACR in the form of two 50-minute appointments each week over a five week period.

It was recognised that there would be some variability in participants' capabilities and the amount of intervention completed. For these purposes, it was decided that participants would complete a minimum of five hours of CACR across the ten sessions, and if they had not reached this standard following ten sessions of CACR, additional appointments would be offered until the amount of intervention was above five hours as recommended by previous research (McGurk et al., 2007).

The current study employed ten Cogpack tasks to comprise a training series that trained attention/vigilance, speed of processing, working memory and visual memory. For each session the ten tasks were presented in the same order and participants were encouraged to complete all of the tasks. All tasks were presented in the permanently adaptive mode where possible. Otherwise tasks were set at the easiest level initially and increased in difficulty after participants achieved approximately 80 per cent accuracy. On completion of each of the ten tasks, participants were presented with comparative scores, which allowed them to track their progress over the course of the intervention period. Individual differences in computer skills and ability resulted in some variation in the number of tasks completed during each session.

Table 3.2: Description of Cogpack tasks used in training series

Name of task	Cognitive function	Description of task
On the road	Attention/vigilance/visual learning	You are driving along a road and have to pay attention to road signs and oncoming traffic.
Sequence	Attention/vigilance	Observe numbers on screen and press a key if the particular rule was met.
Comparisons	Attention/speed of processing	Pairs of strings must be compared. Observe as quickly as possible whether the two match.
Search	Selective attention	Find the number between 1 and 9 hidden in a picture full of symbols as quickly as possible.
Ball	Speed of processing	Move the mouse to bounce the falling balls as many times as possible.
UFO's	Speed of processing	Catch UFOs with the mouse as fast as possible.
Falling stars	Attention/speed of processing	Catch as many falling stars as possible.
Reaction	Speed of processing	Press a button when a critical symbol is displayed on the screen.
Route	Working memory	Make a mental note of the route a black circle takes along a street and retrace it.
Money	Working memory	Decide whether the coins on the screen are enough money to pay the price given.

3.9 Statistical analyses

The MCCB was scored using a computer software programme provided by the distributor, and the T scores were exported into a database using Statistical Package for the Social Sciences (SPSS) software version 19. The UPSA-brief and SFS subtests were scored by the researcher and the raw scores were entered into a Microsoft Excel worksheet developed by the researcher, which computed the adjusted scores appropriately. These scores were then exported into a SPSS database for analyses. All data were analysed using SPSS software version 19. Descriptive analyses were conducted to interpret the demographic information and participant characteristics as follows:

- Number of male and female participants
- Mean age of participants

- Clinical diagnosis
- Current medication
- Inpatient/outpatient status
- Mean number of sessions completed

A combination of parametric and non-parametric statistics was used to investigate the effects of CACR on cognitive functioning, functional capacity and everyday social functioning. The data from the MCCB and the UPSA-brief met the assumptions required to use parametric tests and therefore repeated measures ANOVAs were used to investigate the effects of CACR on cognitive functioning and functional capacity. The data from the SFS did not meet the assumptions required to use parametric tests, therefore, Friedman tests were used to investigate the effects of CACR on social functioning.

CHAPTER 4: JOURNAL ARTICLE

Title

Computer-assisted cognitive remediation in patients with a diagnosis of schizophrenia or schizoaffective disorder: effects on cognition, functional capacity and social functioning.

Running head

CACR: effects on cognition and functioning.

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4.1 Abstract

Background: A recent review found computer-assisted cognitive remediation (CACR) improves cognition in individuals with schizophrenia with a medium effect (Grynszpan et al., 2011).. There is limited research investigating whether the effects of brief CACR interventions are maintained over time and generalise to psychosocial functioning.

Objective: The current study investigated the effects and durability of a brief CACR intervention on cognitive functioning, functional capacity and social functioning.

Method: A repeated measures within-subjects design was conducted to investigate the effects of a five week CACR intervention. Twenty-three individuals with a diagnosis of schizophrenia or schizoaffective disorder participated in the CACR intervention and completed outcome measures assessing cognition, functional capacity and social functioning.

Results: Improvements were observed during the research project in the domains of speed of processing and reasoning/problem solving, as well as the total composite score. When comparing the pre and post-intervention scores no significant effects were observed in cognition, functional capacity or social functioning.

Conclusions: The improvements in speed of processing, reasoning and problem solving and the total composite score could not be solely attributed to the CACR intervention. The findings were in line with previous research which found the effects of a pure CACR intervention do not generalise and lead to improvements in psychosocial functioning.

Chapter 4 it is formatted according to the guidelines for *British Journal of Psychology* (Appendix 1)

4.2 Introduction

4.2.1 Cognitive deficits in schizophrenia

Schizophrenia is a severe mental illness characterised by profound disruptions in thinking, language, experience of emotions and perception (WHO, 2012). There is now substantial evidence supporting the view that cognitive impairment is a pervasive and disabling core feature of schizophrenia (Gold, 2004; Elvevag & Goldberg, 2000). Additionally, research has identified that cognitive deficits in individuals with schizophrenia can impair daily functioning to a greater degree than either positive or negative symptoms (Green, 1996).

Nuechterlein et al. (2004) identified that impairments in speed of processing, attention/vigilance, working memory, verbal learning and memory, visual learning and memory, problem solving and social cognition were frequently found in individuals with schizophrenia. During the onset of symptoms of schizophrenia, there appears to be a period of decline in cognitive functioning, followed by a period of stabilisation (Medalia et al., 2009). Bilder et al. (2000) found a large generalised deficit in neuropsychological functioning of 1.5SD in patients with first-episode schizophrenia, compared to a healthy control group. Additionally, Heaton et al. (2001) reported that level of cognitive impairment in individuals with schizophrenia remained stable despite changes in clinical state, both over a short-term period (mean 1.6 years) and long-term period (mean 5 years).

Green et al. (2000) identified associations between specific cognitive domains and functional outcome measures in individuals with schizophrenia. More specifically, secondary memory was linked with all outcome measures, immediate memory was linked with skill acquisition, executive functions was linked with community functioning and vigilance was linked to skill performance (Green et al., 2000). This highlighted that cognitive functions are related to functional outcome in individuals with a diagnosis of schizophrenia; therefore, treatments aimed at improving cognitive functions may, in turn, improve psychosocial functioning and reduce level of disability in this population.

Further studies have linked cognitive impairments to work performance (Bell et al., 2001), everyday functioning capacity (Twamley et al., 2002) and quality of life (Mohamed et al., 2008). A growing body of literature now demonstrates the direct link between cognitive functioning and psychosocial functioning, as a result there has been an increase in interest in treatments that improve cognitive functioning and whether these effects generalise to psychosocial functioning.

4.2.2 What is cognitive remediation

Wykes and Spaulding (2011) reported that a cognitive remediation experts' workshop defined cognitive remediation therapy for schizophrenia as "a behavioural-training based intervention that aims to improve cognitive processes (attention, memory, executive function, social cognition or metacognition) with the goal of durability and generalisation" (p84). McGurk et al. (2007) conducted a meta-analysis of 26 randomised controlled trials and found that cognitive remediation had

a medium effect (0.41) for overall cognition, a small to medium effect (0.35) for functioning and a small effect (0.28) for symptoms. Computer-assisted cognitive remediation (CACR) may have several advantages over more traditional methods that use paper and pencil tasks; hence there has been a growing interest in CACR recent years.

4.2.3 Effects of CACR on cognitive functioning

To date, only one review of 16 randomised controlled trials has evaluated the effects of CACR on cognition in individuals with a diagnosis of schizophrenia. Grynspan et al. (2011) found results in line with previous reviews of cognitive remediation, reporting that CACR had an effect size of 0.38 on general cognition. Although Grynspan et al. (2011) provided substantial evidence supporting the efficacy of CACR, a number of negative reports have also been published (Murthy et al., 2012; Dickinson et al., 2010). These negative results may have reflected the fact that the intervention only targeted one cognitive domain (Murthy et al., 2012), or that the intervention programme used did not have an established evidence base (Dickinson et al., 2010). These reports of negative results highlight the need for further investigations into the components of successful CACR to inform future treatments.

4.2.4 Effects of CACR on psychosocial functioning

Although there is evidence suggesting that cognitive remediation is effective at improving psychosocial functioning (McGurk et al., 2007), it remains unclear whether the effects of CACR generalise to psychosocial functioning. There is evidence to suggest that CACR can improve social adjustment (Hogarty, 2004),

different aspects of psychosocial functioning (Vita et al., 2010) and quality of life (Cavallaro *et al.*, 2009; Poletti et al., 2010). In addition to these encouraging results, a growing number of articles have found that CACR can significantly improve performance on vocational outcome measures, such as employment status, hours worked and money earned (Bell et al., 2005; Bell et al., 2008; Vauth et al., 2005; Lindenmayer et al., 2008; McGurk et al., 2009).

Despite a growing number of papers reporting that CACR has a positive effect on various measures of psychosocial functioning, a number of papers have also provided negative results. d'Amato et al. (2011) reported that CACR had significant effects on a number of cognitive functions, but these effects did not generalise to social autonomy or quality of life. An additional study conducted by Hermanutz & Gestrich (1991), found no significant effect of CACR on clinicians' ratings of social, occupational and psychological functioning as assessed by the Global Assessment Scale (GAS).

A recent report from the Working Group Conference on Multisite Trial Design for Cognitive Remediation in Schizophrenia (Keefe et al., 2011) highlighted that functional outcome is influenced by a number of factors; therefore, a measure of functional capacity, such as the UPSA-brief, should be included in studies investigating the benefits of cognitive remediation.

4.2.5 Aims of the current study

The current article sought to expand on previous research in a number of ways.

Firstly, the study will employ the MATRICS consensus cognitive battery (MCCB) as an outcome measure for cognitive assessment. The MCCB is a reliable measure that was developed specifically to evaluate cognitive enhancing interventions. It is sensitive to change, and has alternate forms for some subtests to allow for repeat assessment. Previous research has made use of a variety of measures with multiple norms and it has been recommended that future studies would benefit from using the MCCB (Keefe et al., 2011).

In addition to this, the current study aimed to expand the previous literature on the effects of brief CACR interventions, by examining the lasting effects of CACR at a one-month follow-up and by investigating any effects on functional capacity and everyday social functioning. It was hypothesised that CACR would improve cognitive functioning, functional capacity and everyday social functioning.

4.3 Method

4.3.1 Design

The study employed a repeated measures within-subjects design, with participants acting as their own controls. In order to investigate the effects of a brief CACR intervention on cognitive functioning, functional capacity and social functioning, participants completed the outcome measures at four time points throughout the study. All participants were followed up one month post-intervention to investigate any lasting benefits of the intervention.

4.3.2 Participants

Adult participants with a clinical diagnosis of schizophrenia or schizoaffective were recruited for the study through the Adult Mental Health and Psychiatric Rehabilitation services within NHS Grampian. The current study employed the following inclusion/exclusion criteria:

Inclusion

- Participants had to be adults (aged 18 to 64) with a diagnosis of schizophrenia or schizoaffective disorder as classified by the ICD10
- Participants had to be in current contact with services in NHS Grampian
- Participants had to be willing and able to commit to the full intervention
- Participants had to be literate in English language and able to follow on screen instructions
- Participants had to be considered by clinical teams to have capacity to give informed consent.

Exclusion

- Participants were excluded if they were acutely unwell
- Participants were excluded if they were involved in other research projects

4.4 Procedure

All participants were recruited from NHS Psychiatric Rehabilitation and Adult Mental Health services based in Grampian. All participants gave written informed consent prior to their participation. Demographic information was obtained directly

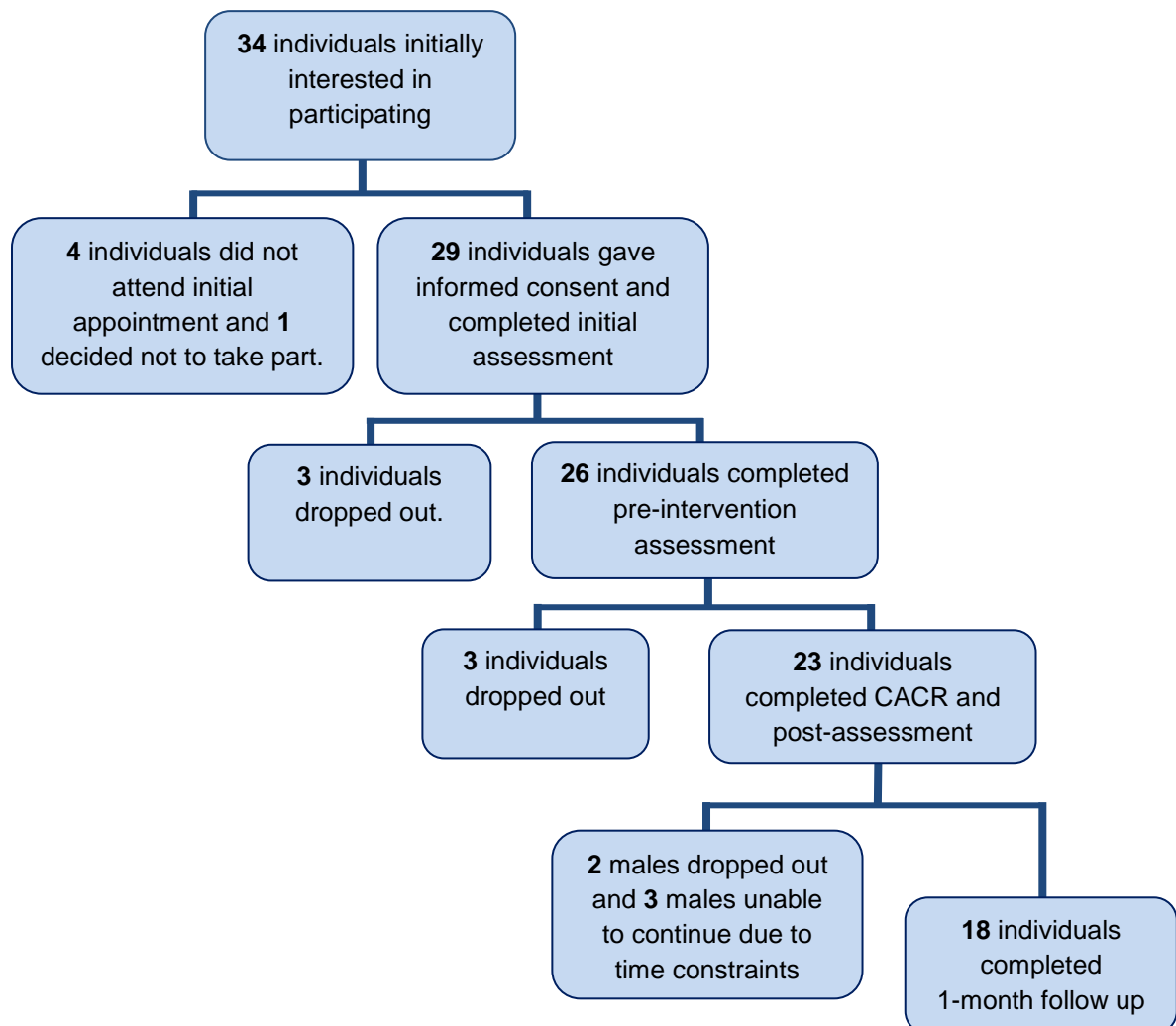
from participants and, with consent from participants, the psychiatrists involved in their care. After completing the baseline assessment, participants entered a four week waiting period, after which they completed the pre-intervention assessment. Participants then engaged in the CACR intervention for approximately 50 minutes, twice a week where possible, for five weeks, with the aim of completing ten sessions in total. After the intervention period, participants completed the post-intervention assessment and were then invited back for a follow-up assessment one month after completing the intervention. At the follow-up appointment all participants were offered the opportunity to receive individual feedback on their performance during their assessments.

4.4.1 Recruitment

Initially thirty-four individuals expressed an interest in taking part; however, only twenty-nine individuals (85 per cent) went on to give informed consent to participate in the study. Three participants dropped out after completing the first assessment (two experienced a deterioration in mental health and one could not commit enough time to complete the intervention). A further three participants dropped out after completing the second assessment (one experienced a deterioration in mental health and two could not commit enough time to complete the intervention). A further two participants dropped out after completing the post-intervention assessment and an additional three participants were not followed up due to time constraints on the study.

In summary, a total of twenty-nine participants completed the initial assessment. Of these, twenty-six completed the pre-intervention assessment, and twenty-three completed both the intervention and the post-intervention assessment. At the time of analysis, one-month follow-up data was available for eighteen participants. Throughout the study, contact was maintained with the consultant psychiatrists responsible for participants' care, to monitor their ongoing mental state and eligibility to participate in the study. The recruitment process and number of participants completing each assessment can be seen in Figure 4.1.

Figure 4.1: Flow chart detailing the recruitment process and dropout rate



4.4.2 Ethical Approval

The methodology of the current study was reviewed by the University of Edinburgh. In addition, ethical approval for the project was also obtained from the North of Scotland Research ethics Service (NRES) and local approval was also obtained from the NHS Grampian Research and Development department.

4.5 Assessment

Demographic information was collected once participants had given informed written consent. Participants were assessed using the three outcome measures: Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery (MCCB), University of California in San Diego (UCSD) Performance Based Skills Assessment-Brief (UPSA-brief) and three subtests from the Social Functioning Scale (SFS). The outcome measures were completed at baseline, pre-intervention, post-intervention and at one-month follow-up. The assessments were completed by a trainee clinical psychologist, who also ran the CACR intervention sessions.

4.5.1 Cognitive Functioning

The MCCB was specifically developed to measure change in trials of cognition enhancing interventions. It is considered to be an acceptable standard for measuring cognition in clinical trials of participants with a diagnosis of schizophrenia (Keefe et al., 2011). The MCCB assesses cognitive functioning across seven domains, through ten subtests. Raw scores are converted to adjusted T-scores for the seven cognitive domains and a total composite score. Reported test-retest reliabilities for the subtests

of the MCCB were considered good, with the majority of tests obtaining an r value above 0.70 (Nuechterlein et al., 2008). In addition to this, alternative forms are available for a number of the subtests, to minimise practice effects during multiple assessments over time. The MCCB has been demonstrated as a valid and sensitive measure of cognitive impairment in schizophrenia, which is related to functional outcome (August et al., 2011).

4.5.2 Functional capacity

The UPSA-brief was designed to assess financial and communication skills in community based individuals with schizophrenia. Each of the two subscales gives a maximum score of 50 points, which are combined to give a total score ranging from 0 to 100 points; higher scores reflect higher levels of functional capacity. The test-retest reliability of the UPSA-brief was investigated by Leifker et al. (2010), who found that the reliability of the UPSA-brief ranged from $r=.66$ to $r=.81$ for periods of up to 36 months. In addition to this, it has been demonstrated that the UPSA correlates with cognitive functioning as measured using the MCCB, $r=.61$ (Green et al., 2008).

4.5.3 Social functioning

The Social Functioning Scale (SFS) was developed to assess seven domains of functioning that are considered crucial for community functioning (Birchwood et al., 1990). Items are scored on a four point scale, with higher scores reflecting a higher level of functioning. The raw scores of the seven domains are converted into a scaled score with a mean of 100 and standard deviation of 15. In the current study,

three subtests were administered: social engagement/withdrawal, independence-performance and independence-competence. Birchwood et al. (1990) reported high internal reliability (alpha of 0.80) and inter-rater reliability (0.94). Additionally, the SFS was recently identified as a superior assessment of social functioning, according to a project funded by the National Institute of Mental Health, which aimed to enhance the measurement of real world outcomes through the evaluation of functioning measures (Leifker et al., 2011). Previous research has demonstrated that scores on the SFS are significantly correlated with neuropsychological test performance (Dickerson et al., 1996).

4.6 Intervention

Cogpack professional software (version 8.34) is a computerised cognitive remediation package that was developed in Germany. It has been clinically tested in psychiatric populations throughout Europe, since 1986. The current version used in the study consisted of 64 programmes that can be used to train various cognitive skills including: visuomotor, comprehension, reaction, vigilance, memory, language, intellectual and professional skills (Marker, 2011). A number of studies have reported that Cogpack interventions can significantly improve cognitive functioning (McGurk et al., 2005; Cavallero et al., 2009; Sartory et al., 2005; Vauth et al., 2005; Wolwer et al., 2005; Lindenmayor et al., 2008) and daily functioning (McGurk et al., 2005; Cavallero et al., 2009, Poletti et al., 2010).

In the current study, the intervention consisted of a standardised CACR training series, which consisted of ten tasks targeting attention/vigilance, speed of processing,

working memory and visual learning. For each session, the tasks were presented in the same order and participants were encouraged to complete all of the tasks. On completion of each task, participants were presented with comparative scores, which allowed them to track their progress over the course of the intervention period. Where possible, the Cogpack training series was presented in the permanently adaptive mode, to adjust to the performance of each participant and reduce any sense of failure. The training took place either individually or in small groups of up to three participants with each participant working on their own computer.

4.7 Statistical analyses

Statistical Package for Social Sciences (SPSS) version 19 was used to analyse the data. Exploratory analyses of the distribution of the data were conducted to investigate whether the data met the assumptions required to use parametric tests. A combination of parametric and non-parametric tests was employed to investigate any changes in cognitive functioning, functional capacity and social functioning across the four time points.

4.8 Results

4.8.1 Group characteristics

Of the thirty-four people who initially showed an interest in participating, twenty-nine participants completed the baseline assessment, twenty-six completed the pre-intervention assessment and twenty-three completed the CACR intervention and post-intervention assessment. At the time of analysis, one-month follow-up data was available for eighteen participants. Demographic information for the twenty-three

participants who engaged in the CACR intervention can be seen in table 4.1.

Participants completed between 250 and 480 minutes of CACR (M = 357; SD = 63.5). The total number of CACR sessions completed by participants ranged between 6 and 11 sessions (M = 8.6; SD = 1.44).

Table 4.1: Demographics and clinical characteristics of participants who engaged in CACR (n=23)

Variable	N	%
Gender		
Male	18	78
Female	5	22
Antipsychotic medication		
Typical	6	26
Atypical	17	74
Clinical diagnosis		
Schizophrenia	13	57
Paranoid schizophrenia	7	30
Schizoaffective disorder	3	13
Participant status		
Inpatient	6	26
Outpatient	17	74
	Mean	SD
Age (years)	49.9	9.08
Intervention		
Number of sessions	8.6	1.44
Total time training (minutes)	357	65.5

The sample consisted of eighteen males (78 per cent) and five females (22 per cent).

The age of the participants ranged from twenty-five to sixty-one (M = 49.9; SD = 9.08). Thirteen participants (57 per cent) had a clinical diagnosis of schizophrenia, seven (30 per cent) had a diagnosis of paranoid schizophrenia and three (13 per cent) had a diagnosis of schizoaffective disorder. Six inpatients (26 per cent) and

seventeen community outpatients (74 per cent) participated in the current study. Of the twenty-three participants, six (26 per cent) were being treated with typical antipsychotics. The remaining seventeen participants (74 per cent) were being treated with atypical antipsychotics.

4.8.2 Investigations of assumptions of normality

Descriptive data and histograms (appendix 10) for each of the main variables were analysed in order to establish whether the data met the assumptions required to use parametric tests. Field (2005) reported that in a small sample, a z score of skewness above 2.58 (or below -2.58) indicates that the degree of skewness is too large to meet the assumptions required to employ parametric tests. Examination of z scores revealed that the data from two outcome measures: the MCCB and the UPSA-brief, appeared to meet the assumptions required to use parametric tests, therefore, repeated measures ANOVAs were used to investigate the effects of a five-week CACR intervention on cognitive functioning as assessed by the MCCB, and functional capacity as assessed by the UPSA-brief. However, the data from the SFS did not meet the assumptions required to use parametric tests and therefore Friedman tests were used to investigate the effects of CACR on social functioning as assessed by the SFS.

4.8.3 Bonferroni correction

It is recognised that when conducting multiple comparisons there is an increased likelihood of finding a significant effect by chance alone (Field, 2005). A Bonferroni correction controls for such errors, by dividing the significance level by the number of comparisons being carried out. As the current study conducted multiple

comparisons, Bonferroni adjustments were employed in order to reduce the risk of Type I errors.

4.8.4 Treatment effects on cognitive functioning

Performance on the MCCB was assessed by calculating T scores for the seven cognitive domains and the total composite score. Table 4.2 provides descriptive statistics for the scores obtained at the four assessments. Repeated measures ANOVAs were conducted to investigate whether a five-week CACR intervention improved performance in any of the seven cognitive domains and the total composite score. As multiple analyses were being conducted, effects were examined with a Bonferroni adjustment for the eight analyses, setting the alpha level at 0.00625 (0.05/8). Further post hoc investigations of main effects were conducted using pairwise comparisons with a Bonferroni adjustment.

Table 4.2: Descriptive analysis of T scores obtained on the MCCB domains during assessments.

MCCB domain	Baseline n=29	Pre-intervention n=26	Post-intervention n=23	1-month follow up n= 18
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Speed of Processing	29.7 (10.91)	35.9 (9.75)	36.7 (10.46)	36.7 (10.72)
Attention/Vigilance	34.2 (12.00)	38.6 (13.11)	37.5 (12.92)	38.9 (12.71)
Working Memory	31.5 (12.73)	36.7 (12.66)	34.9 (14.70)	35.8 (14.31)
Verbal Learning	34.3 (8.43)	35.4 (9.22)	37.5 (8.89)	36.6 (8.50)
Visual Learning	32.9 (13.83)	34.6 (16.07)	35.2 (14.17)	39.3 (14.33)
Reasoning/Problem Solving	35.6 (7.44)	39.5 (7.18)	40.7 (9.29)	41.1 (7.73)
Social Cognition	33.6 (9.49)	33.7 (10.54)	36.1 (10.53)	32.6 (11.29)
Composite Score	22.7 (12.96)	27.1 (13.15)	31 (12.57)	31.7 (12.89)

MCCB: The NIMH Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) consensus cognitive battery.

Speed of processing

The descriptive analyses highlighted that the highest mean T scores were obtained post-intervention and at the one-month follow up. The results of the repeated measures ANOVA, examined with a Bonferroni adjustment, revealed that mean T scores on the speed of processing domain differed significantly between the four assessments ($F(3, 48) = 8.741, p = .005, \eta^2_p = .35$).

Post hoc pairwise comparisons with a Bonferroni adjustment (appendix 11) revealed that, compared to baseline, participants performed significantly better on the speed of processing domain at post-intervention ($p = .004$) and at one-month follow-up ($p = .002$). No other significant differences were found. Although these results indicate a significant improvement in the speed of processing domain during the course of the research, pairwise comparisons revealed no significant difference between mean T scores obtained at the pre-intervention assessment and the post-intervention assessment. Therefore, these findings did not support the hypothesis that a CACR intervention would improve cognitive functioning.

Attention/vigilance

The descriptive analyses highlighted that the lowest mean T score was obtained on the baseline assessment, while the highest was obtained at the one-month follow up assessment. The greatest increase in T scores occurred between the baseline assessment and the pre-intervention assessment. The results of a repeated measures ANOVA, examined with a Bonferroni adjustment, revealed no significant difference in mean T scores on the attention/vigilance domain between the four assessments (F

(3,42) = 1.082, $p = .367$, $\eta^2_p = .07$). This finding did not support the hypothesis that a CACR intervention would improve cognitive functioning.

Working memory

The descriptive analyses highlighted that the lowest mean T score for the working memory domain was obtained at the baseline assessment, while the highest was obtained at the pre-intervention assessment. The results of the repeated measures ANOVA, examined with a Bonferroni adjustment, revealed no significant difference in mean T scores on the working memory domain between the four assessments ($F(3, 48) = 2.328$), $p = .086$, $\eta^2_p = .13$). This finding did not support the hypothesis that a CACR intervention would improve cognitive functioning.

Verbal learning

The descriptive analyses highlighted that the lowest mean T score for the verbal learning domain was obtained at the baseline assessment, while the highest was obtained at the post-intervention assessment. These scores suggest that there may have been some improvement in performance on the verbal learning domain following the intervention. However, the results of the repeated measures ANOVA, examined with a Bonferroni adjustment, revealed no significant difference in mean T scores on the verbal learning domain between the the four assessments ($F(3, 48) = .499$), $p = .685$, $\eta^2_p = .03$). This finding did not support the hypothesis that a CACR intervention would improve cognitive functioning.

Visual learning

The descriptive analyses highlighted that the lowest mean T score for the verbal learning domain was obtained at the baseline assessment, while the highest was obtained at the one-month follow up assessment. These scores suggest that there may have been some improvement in performance on the visual learning domain following the intervention. The results of the repeated measures ANOVA, examined with a Bonferroni adjustment, revealed no significant difference in mean T scores on the visual learning domain between the four assessments ($F(3, 45) = 2.970, p = .042, \eta^2_p = .17$). This finding did not support the hypothesis that a CACR intervention would improve cognitive functioning.

Reasoning/problem solving

The descriptive analyses highlighted that the lowest mean T score for the reasoning/problem solving domain was obtained at the baseline assessment, while the highest was obtained at the one-month follow up assessment. These scores suggest that there may have been some improvement in performance following the intervention. The results of the repeated measures ANOVA, examined with a Bonferroni adjustment, revealed a significant difference in mean T scores on the on the reasoning/problem solving domain between the four assessments ($F(3, 48) = 9.501, p = .005, \eta^2_p = .37$).

Post hoc pairwise comparisons with a Bonferroni adjustment (appendix 11) revealed that, compared to baseline, participants performed significantly better on the reasoning/problem solving domain at post-intervention ($p = .005$) and at one-month

follow-up ($p=.001$). No other significant differences were found. Although these results indicate a significant improvement in the reasoning/problem solving domain during the course of the research, pairwise comparisons found no significant difference between scores obtained on the pre-intervention assessment and the post-intervention assessment scores. Therefore, these findings did not support the hypothesis which stated that a CACR intervention would improve cognitive functioning.

Social cognition

The descriptive analyses highlighted that the lowest mean T score for the social cognition domain was obtained at the one-month follow up assessment, while the highest was obtained at the post-intervention assessment. The results of the repeated measures ANOVA, examined with a Bonferroni adjustment, revealed no significant difference in mean T scores on the social cognition domain between the four assessments ($F(3,442) = .954, p = .423, \eta^2_p = .06$). This finding did not support the hypothesis that a CACR intervention would improve cognitive functioning.

Total composite score

The descriptive analyses highlighted that the lowest mean T score for the overall composite score was obtained at the baseline assessment, while the highest was obtained at the one-month follow up assessment. The results of the repeated measures ANOVA, examined with a Bonferroni adjustment, revealed a significant difference in the mean composite scores obtained at the four assessments ($F(3, 33) = 8.178, p = .005, \eta^2_p = .43$).

Post hoc pairwise comparisons with a Bonferroni adjustment (appendix 11) revealed that, compared to baseline, participants' total composite scores were significantly higher at post-intervention ($p = .018$), and at one-month follow-up ($p = .005$). Additionally, participants' total composite scores were significantly higher at the one-month follow-up assessment compared to the pre-intervention assessment ($p=.046$). No significant difference was found between the total composite scores obtained at the pre-intervention and the post-intervention assessment.

These results suggest that total composite scores for the MCCB did improve significantly during the course of the research project, although there was not a significant improvement in scores obtained at the post-intervention compared to the pre-intervention assessments. These findings may provide some support for the hypothesis that a CACR intervention would improve cognitive functioning.

4.8.5 Treatment effects on functional capacity

Performance on the UPSA-brief was assessed by converting the raw subtest scores to an adjusted score based on a 50-point scale. The total score was then calculated by converting the raw score to an adjusted score based on a 100-point scale, with higher scores reflecting higher levels of functioning. As can be seen from Table 4.3, the lowest total mean score was obtained at baseline, while the highest total mean score was obtained at the post-intervention assessment.

Table 4.3: Descriptive analysis of adjusted scores obtained on the UPSA-brief during assessments.

	Baseline n=28	Pre-intervention n=25	Post-intervention n=23	1-month follow up n= 18
UPSA-b score	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Total score ^a	55.6 (17.52)	60.4 (19.61)	61.4 (21.20)	61.8 (21.05)
Financial ^b	31.9 (11.17)	32.0 (10.94)	33.2 (19.56)	32.8 (11.98)
Communication ^b	23.6 (9.87)	28.4 (11.60)	29.2 (11.74)	29.0 (11.68)

UPSA-b: The University of California in San Diego (UCSD) Performance Based Skills Assessment - brief

a converted to a 100-point scale with higher scores reflecting higher levels of functioning

b converted to a 50-point scale with higher scores reflecting higher levels of functioning

Repeated measures ANOVAs were conducted to investigate whether a five-week CACR intervention improved performance in either of the two subtests and the total UPSA-brief score. As multiple analyses were being conducted, effects were examined with a Bonferroni adjustment for the three analyses, setting the alpha level at 0.01666 (0.05/3).

The results of the repeated measures ANOVAs, examined with Bonferroni adjustments, revealed no significant differences in mean scores between the four assessments, on the financial subtest ($F(3, 51) = .132, p = .941, \eta^2 = .008$), the communication subtest ($F(3, 51) = 2.400, p = .079, \eta^2 = .12$), or the UPSA-brief total score ($F(3, 51) = 2.054, p = .118, \eta^2 = .11$). These findings provided no evidence to support to the hypothesis that a five-week CACR intervention would improve functional capacity as assessed by the UPSA-brief.

4.8.6 Treatment effects on social functioning

Performance on the SFS subtests was assessed by calculating the raw subtest scores and converting them to an adjusted score with a mean of 100 and SD of 10, with

higher scores reflecting higher levels of functioning. Table 4.5 provides descriptive statistics for the scores obtained on the SFS at the four assessments.

Table 4.4: Descriptive analysis of adjusted scores obtained on the SFS during assessments.

	Baseline n=29	Pre-intervention n=25	Post-intervention n=20	1-month follow up n= 18
SFS scaled scores a	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
Withdrawal	97 (91, 100)	97 (89, 105)	100 (94, 105)	98 (93, 105)
Independence competence	107 (98, 112)	107 (96, 114)	107 (104, 114)	104 (96, 115)
Independence performance	107 (102, 110)	107 (99, 110)	107 (101, 110)	109 (103, 111)

SFS: Social Functioning Scale

a. converted to a scaled score with a mean of 100 and SD 10.

Friedman tests were conducted to investigate whether a five-week CACR intervention improved performance in any of the three subscales of the SFS. As multiple analyses were conducted, effects were examined with a Bonferroni adjustment for the three analyses, setting the alpha level at 0.01666 (0.05/3). The Friedman tests revealed no significant differences in scaled scores between assessments on the withdrawal subscale ($X^2(3) = 6.258, p = .098$), the independence-performance subscale ($X^2(3) = 4.232, p = .240$), or the independence-competence subscale ($X^2(3) = 2.379, p = .511$). These findings provided no evidence to support the hypothesis that a five-week CACR intervention would improve social functioning as assessed by the SFS.

4.9 Discussion

This study aimed to evaluate the effects of a brief CACR intervention on cognitive functioning, functional capacity and social functioning in patients with schizophrenia

or schizoaffective disorder. The study employed the gold standard tool for assessing cognitive functioning across time, and followed recommendations set out by experts in the field to include a measure of functional capacity (Keefe *et al.*, 2011). The participants received up to eight hours of training over a five week period and all participants except one completed more than five hours of training; the minimum number of hours shown to be effective in this population (McGurk *et al.* 2007).

Three outcome measures were assessed during this study: neuropsychological tests that were not related to any of the training exercises (MCCB), a measure of functional capacity (UPSA-brief) and a measure of real world social functioning (SFS).

The numbers needed for a control group were not attainable in the current research, therefore, participants acted as their own controls. The descriptive analyses highlighted an increase in mean T scores between the baseline assessment and the pre-intervention assessment on all of the seven cognitive domains and the total composite score on the MCCB. These increases may reflect practice effects associated with the MCCB. However, further statistical analyses revealed no significant differences between any of the T scores obtained on the MCCB at the baseline assessment and the pre-intervention assessment. Similarly, although there was an increase in the adjusted scores obtained on the UPSA-brief at the pre-intervention assessment compared to the baseline assessment, these changes were not statistically significant.

The time scale of the current research resulted in just four weeks between assessments. Although the increases in T scores between the baseline assessment and the pre-intervention assessments were not statistically significant, this time scale would have benefited from being increased in order to reduce any associated practice effects of repeated assessments.

4.9.1 Patient experience

Generally, patients engaged well with the CACR intervention and reported feeling a sense of enjoyment from completing the computer tasks. Only one patient requested to stop the intervention prior to completing the minimum recommended 300 minutes, due to difficulties travelling to the hospital. Qualitative feedback from participants indicated that more variation in the tasks being completed would have been preferred. It was noted that the current research project aimed to evaluate a standardised treatment that consistent of 10 separate tasks, but a more varied approach that is tailored to individual's cognitive weaknesses could be implemented if the intervention was introduced into local services.

4.9.2 Effects on cognition

When comparing the pre-intervention and post-intervention T scores obtained on the seven cognitive domains and the total composite score, the current study found no evidence of any benefits of a brief CACR intervention on cognitive functioning. Previous research has reported that CACR has a medium effect ($d = 0.38$) on general cognition (Grynszpan, 2010), and that a minimum of five hours of cognitive remediation may be sufficient to improve cognition (McGurk et al., 2007). Field

(1997) found that six sessions of CACR did not improve attention in individuals with schizophrenia. In the current study, participants completed an average of 5.95 hours, which is a similar dose to that offered by Field (1997). Taken together, these findings suggest that six hours of CACR is not sufficient to improve cognitive functioning in this population.

Hermanutz & Gestrich (1991) found that eight sessions was sufficient to improve cognition, while Medalia (2001) reported a significant effect on problem solving skills in individuals with schizophrenia following ten sessions of CACR. It was acknowledged that the amount of intervention offered in the current study was relatively low in comparison to the amount offered in the existing published research. It may be that the dose of intervention in the current study was just below what is needed to improve cognitive functioning. However, the findings of the current study supplement the existing literature reporting negative results for brief CACR interventions (Field, 1997) and longer-term CACR interventions (Murthy et al., 2012; Dickinson et al., 2010).

Despite the lack of improvement in scores from pre-intervention to post intervention, the current study did find significant improvements in two of the seven cognitive domains, as well as the total composite scores. It is worth noting that scores on the speed of processing and the reasoning/problem solving domain, were significantly better at the one-month follow-up and the post-intervention assessment than the scores obtained at baseline. These findings highlight that both speed of processing and reasoning/problem solving improved during the course of the research; therefore,

the CACR intervention may have provided some benefit on cognition. Although encouraging, these improvements in scores can not be solely attributed to the CACR intervention, as no significant differences in performance were found between scores obtained at the pre-intervention and the post-intervention assessments.

Interestingly, the mean total composite score, at both the one-month follow-up and the post-intervention assessment, was significantly higher than the mean score at baseline. Furthermore, the participants' total composite score was significantly higher at the one-month follow-up compared to the pre-intervention assessment. These findings indicate that there was an improvement in overall cognition during the course of the research project.

To calculate a total composite score, participants had to complete all 10 subtests of the MCCB. Five participants refused to complete a subtest on the MCCB and therefore the total composite scores, at all four assessment points, were only available for thirteen participants. Medalia & Richardson (2005) highlighted that intrinsic motivation was an important factor in predicting successful responses to CACR. It is possible that the thirteen individuals who completed all MCCB subtests had higher motivation and, as a result, had a more positive treatment outcome on general cognition. Future research into CACR involving measures of motivation may be an interesting addition to the literature.

4.9.3 Effects on psychosocial functioning

The results of the current study found that CACR did not significantly improve functional capacity or social functioning in individuals with schizophrenia or schizoaffective disorder. With regards to the UPSA-brief, Leifker et al. (2010) identified that relatively large changes in raw scores (21.32, SD 1.06) would be required between assessments to exceed a 90 per cent confidence interval and reflect a true change in functional capacity. Although there was some improvement in mean scores obtained on the UPSA-brief across assessments, these changes were not statistically significant, and did not exceed the improvement suggested by Leifker et al. (2010). Similarly, there were no observed improvements on any of the three subscales of the SFS.

Only a small number of studies have investigated the effects of brief CACR interventions, and only one study (Hermanutz & Gestrich, 1991) was found that investigated whether any effects of CACR generalise to functional outcome. The results of the current study are in line with previous findings and suggest that a brief CACR intervention cannot significantly improve psychosocial functioning on its own. Additionally, the findings here also reflect those reported by Murthy et al. (2012) and Dickinson et al. (2010), as CACR did not improve functional capacity in individuals with schizophrenia or schizoaffective disorder.

Bowie et al., (2012) investigated whether the effects of a CACR intervention generalised to functional capacity and real world functioning when offered as a pure intervention and when combined with a functional skills intervention. The results

highlighted that improvement in functional capacity was greater following a combined treatment, however, improvement in real world functioning was not observed following a pure CACR intervention (Bowie et al., 2012). Previous literature suggests that the positive effects of CACR generalise to psychosocial functioning when it is offered as part of a wider intervention, such as vocational rehabilitation (Bell et al., 2005; Bell et al., 2008; Vauth et al., 2005; McGurk et al., 2009) or functional skills training (Bowie, 2012).

The current study offered a pure CACR intervention, hence it adds to previous literature reporting that pure CACR interventions do not improve functional capacity or everyday functioning (Hermanutz & Gestrich, 1991; Murthy et al., 2012; Dickinson et al., 2010; Bowie et al., 2012). Offering CACR as part of a wider intervention was beyond the scope of the current project, but it was recognised that future research would benefit from comparing the effects of offering CACR as part of a wider intervention.

4.9.4 Patient characteristics

Many of the participants in the current study were recruited through the severe and enduring service and had experienced chronic mental health difficulties for prolonged periods of time. Medalia & Richardson (2005) found that individuals rated as less impaired on the PANSS made greater improvements after CACR interventions. The lack of findings in the current study may reflect a greater degree of impairment in the individuals that participated, in comparison to participants in other studies. It may be that individuals, who are considered to have a greater degree

of impairment do not benefit from brief interventions, but require CACR with a longer duration to gain any benefits.

There is also some evidence indicating that cognitive remediation may be more beneficial when offered to individuals during the prodromal stage of schizophrenia as an early intervention (Rauchensteiner et al., 2011). Future research would benefit from investigating participant characteristics further, in order to establish whether there is an optimum time for offering CACR and whether some individuals are more likely to benefit than others (Wykes & Spaulding, 2011).

Due to the anticipated difficulties in recruitment, and the relatively short time frame for completion of the project, the current study did not employ stringent inclusion and exclusion criteria, therefore, confounding variables may have impacted on participants' scores on the outcome measures. Comparative research has tended to recruit participants who are deemed to be stable on medication for a specified time period, although the criterion for defining this varies considerably between studies. It was acknowledged that changes in medication, mental state fluctuation or substance misuse could have impacted on participants' cognitive functioning in the current study. More stringent inclusion/exclusion criteria would have been beneficial to conduct a more rigorous investigation and draw firmer conclusions about the effects of CACR.

4.9.5 Intervention characteristics

Previous research has identified that between five and fifteen hours of cognitive remediation was sufficient to improve cognition in individuals with schizophrenia or schizoaffective disorder. However, the findings of the current study, along with previous research conducted by Field (1997), suggest that a brief CACR intervention on its own does not improve cognition in this population. Keefe et al. (2011) defined a short-term trial of cognitive remediation as a twelve-week intervention. The results of the current study along with this definition, would suggest that brief interventions need to be longer than the five week period employed in this research, to significantly improve cognitive functioning.

The current study aimed to investigate the effects of a brief five week CACR intervention, which consisted of two 50 minute sessions per week. Medalia and Richardson (2005) found that individuals who completed a high intensity intervention (less than 128 days) benefited with a large effect ($d = 1.46$), compared to those who completed a lower intensity intervention (more than 128 days), who benefited with a smaller effect ($d = .26$). Medalia and Richardson (2005) also reported that CACR was required to be offered twice a week in order to see gains. Although this was the intention of the current study, it was noted that the majority of participants missed at least one session and it proved difficult to maintain this intensity level throughout. Therefore, future research may benefit from offering the intervention three times per week, to allow for potential missed appointments. It was recognised that the intervention used in the current study may have been more successful if the intensity of the intervention had been increased.

The current study offered a relatively brief CACR intervention in comparison to much of the published research, and the views of Keefe et al. (2011) who defined a brief cognitive remediation intervention as lasting for 12-weeks. Although it is of great clinical benefit to establish whether a brief intervention can improve cognition and psychosocial functioning in individuals with schizophrenia or schizoaffective disorder, the findings of the current study suggest that the intervention used was too short to foster any observable gains between in the scores obtained at pre-intervention and post- intervention. The current study also used a standard training series for all participants, to allow for the evaluation of a particular training series. Employing CACR within clinical settings would involve developing personalised training series' to address each individual's cognitive weaknesses. The current study may have also benefited from tailoring the training series to each participant, rather than relying on a set training series.

Finally, this study may have been slightly underpowered. The original power calculation required twenty-four participants to complete the entire project, although twenty-three participants completed the intervention and post-intervention assessment, only eighteen participants completed the one-month follow up.

4.9.6 Strengths and limitations of the study

The current study adds to the evidence base by investigating the effects and durability of a brief CACR intervention on cognition and psychosocial functioning. A clear strength of the current study was that it employed outcome measures that are considered to be among the gold standard in the field. Additionally, care was taken

to ensure the training series did not make use of tasks similar to those used in the MCCB, in order to avoid any potential effects being the result of an underlying practice effect.

The current study had a number of limitations. It was not possible to employ any form of blinding techniques, as such, both the participants and the assessor were aware of the purpose of the study and the purpose of assessment at each time point. This is a clear weakness of the project, but formal blinding techniques were beyond the scope of the current project due to staffing limitations.

The inclusion/exclusion criteria for the current study were kept relatively broad due to perceived difficulties of recruitment. This resulted in two participants with current substance misuse difficulties being enrolled in the study. Additionally, the researcher was aware that mental state fluctuated in some participants during the course of the research and that medication did not remain stable in all participants throughout the duration of the research. Such confounding variables may have little impact on long-term trials but could affect the results of brief intervention studies.

4.10 Conclusions

The current study aimed to evaluate the effects of a brief CACR intervention on cognitive functioning as assessed by the MCCB, on functional capacity as assessed by the UPSA-brief and on social functioning as assessed by the SFS. The results of the study found no significant effect of CACR on any of the three outcome measures between the pre-intervention and the post-intervention assessments. However,

improvements were observed over the course of the research on the domains of speed of processing, reasoning and problems solving, as well as the total composite score. The results suggest that a brief CACR intervention was not effective at improving cognitive functioning, functional capacity or social functioning in individuals with schizophrenia or schizoaffective disorder. Further studies investigating the effects of CACR would benefit from examining participant characteristics and offering CACR as part of a wider psychosocial intervention. Additionally, future studies may benefit from offering a longer intervention period.

Journal Article References

- August, S., Kiwanuka, J., McMahon, R., & Gold, J. (2012). The MATRICS consensus cognitive battery (MCCB): Clinical and cognitive correlates. *Schizophrenia Research, 134*(1), 76-82.
- Bell, M., Bryson, G., Greig, T., Fiszdon, J., & Wexler, B. E. (2005). Neurocognitive enhancement therapy with work therapy: Productivity outcomes at 6- and 12-month follow-ups. *Journal of Rehabilitation Research and Development, 42*, 829-838.
- Bell, M. D., & Bryson, G. (2001). Work rehabilitation in schizophrenia: Does cognitive impairment limit improvement? *Schizophrenia Bulletin., 27*, 269-279.
- Bell, M. D., Zito, W., Greig, T., & Wexler, B. E. (2008). Neurocognitive enhancement therapy with vocational services: Work outcomes at two-year follow-up. *Schizophrenia Research, 105*(1-3), 18-29.
- Bilder, R. M., Goldman, R. S., Robinson, D., Reiter, G., Bell, L., Bates, J. A. et al. (2000). Neuropsychology of first-episode schizophrenia: Initial characterization and clinical correlates. *American Journal of Psychiatry, 157*(4), 549-559.
- Birchwood, M., Smith, J., Cochrane, R., Wetton, S., & Copestake, S. (1990). The social functioning scale. the development and validation of a new scale of social adjustment for use in family intervention programmes with schizophrenic patients. *The British Journal of Psychiatry, 157*(6), 853-859.

- Bowie, C. R., McGurk, S. R., & Mausbach, B., Patterson, T.L., & Harvey, P.D. (2012). Combined cognitive remediation and functional skills training for schizophrenia: Effects on cognition, functional competence, and real-world behavior. *American Journal of Psychiatry, 169*, 710-718.
- Cavallaro, R., Anselmetti, S., Poletti, S., Bechi, M., Ermoli, E., Cocchi, F. et al. (2009). Computer-aided neurocognitive remediation as an enhancing strategy for schizophrenia rehabilitation. *Psychiatry Research, 169*(3), 191-196.
- Cogpack (version 8.34). (2012). *Technical manual*. Ladenburg: Marker.
- d'Amato, T., Bation, R., Cochet, A., Jalenques, I., Galland, F., Giraud-Baro, E. et al. (2011). A randomized, controlled trial of computer-assisted cognitive remediation for schizophrenia. *Schizophrenia Research, 125*(2-3), 284-290.
- Dickerson, F., Boronow, J. J., Ringel, N., & Parente, F. (1996). Neurocognitive deficits and social functioning in outpatients with schizophrenia. *Schizophrenia Research, 21*(2), 75-83.
- Dickinson, D., Tenhula, W., Morris, S., Brown, C., Peer, J., Spencer, K. et al. (2010). A randomized, controlled trial of computer-assisted cognitive remediation for schizophrenia. *American Journal of Psychiatry, 167*(2), 170-180.
- Ellevåg, B., & Goldberg, T. E. (2000). Cognitive impairment in schizophrenia is the core of the disorder. *Critical Reviews in Neurobiology, 14*(1), 1-21.

- Field, A. (2005). *Discovering statistics using SPSS* (2nd ed.). London: SAGE publications.
- Field, C. D., Galletly, C., Anderson, D., & Walker, P. (1997). Computer-aided cognitive rehabilitation: Possible application to the attentional deficit of schizophrenia, a report of negative results. *Perceptual and Motor Skills*, 85(3), 995-1002.
- Gold, J. M. (2004). Cognitive deficits as treatment targets in schizophrenia. *Schizophrenia Research*, 72(1), 21-28.
- 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”? *Schizophrenia Bulletin*, 26(1), 119-136.
- Green, M. F. (1996). What are the functional consequences of neurocognitive deficits in schizophrenia? *The American Journal of Psychiatry*, 153(3), 321-330.
- Green, M.F., Nuechterlein, K.H., Kern, R.S., Baade, L.E., Fenton, W.S., Gold, J.M. et al. (2008). Functional co-primary measures for clinical trials in schizophrenia: Results from the MATRICS psychometric and standardization study. *American Journal of Psychiatry*, 165, 221-228.
- 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. *Psychological Medicine: A Journal of Research in Psychiatry and the Allied Sciences*, 41(1), 163-173.

- Heaton, R.K., Gladsjo, J.A., Palmer, B. W., Kuck, J., Marcotte, T.D., & Jeste, D.V. (2001). Stability and course of neuropsychological deficits in schizophrenia. *Archives of General Psychiatry*, 58, 24-32.
- Hermanutz, M., & Gestrich, J. (1991). *European Archives of Psychiatry and Clinical Neuroscience*, 240(4), 282-287.
- Hogarty, G. E., Flesher, S., Ulrich, R., Carter, M., Greenwald, D., Pogue-Geile, M. et al. (2004). Cognitive enhancement therapy for schizophrenia: Effects of a 2-year randomized trial on cognition and behavior. *Archives of General Psychiatry*, 61(9), 866-876.
- Keefe, R. S. E., Vinogradov, S., Medalia, A., Silverstein, S. M., Bell, M. D., Dickinson, D. et al. (2011). Report from the working group conference on multisite trial design for cognitive remediation in schizophrenia. *Schizophrenia Bulletin*, 37(5), 1057-1065.
- Leifker, F. R., Patterson, T. L., Heaton, R. K., & Harvey, P. D. (2011). Validating measures of real-world outcome: The results of the VALERO expert survey and RAND panel *Schizophrenia Bulletin*, 37(2), 334-343.
- Leifker, F. R., Patterson, T. L., Bowie, C. R., Mausbach, B. T., & Harvey, P. D. (2010). Psychometric properties of performance-based measurements of functional capacity: Test–retest reliability, practice effects, and potential sensitivity to change. *Schizophrenia Research*, 119(1-3), 246-252.

- Lindenmayer, J., McGurk, S. R., Mueser, K. T., Khan, A., Wance, D., Hoffman, L. et al. (2008). A randomized controlled trial of cognitive remediation among inpatients with persistent mental illness. *Psychiatric Services, 59*(3), 241-247.
- McGurk, S. R., Mueser, K. T., DeRosa, T. J., & Wolfe, R. (2009). Work, recovery, and comorbidity in schizophrenia: A randomized controlled trial of cognitive remediation. *Schizophrenia Bulletin, 35*(2), 319-335.
- McGurk, S. R., Twamley, E. W., Sitzer, D. I., McHugo, G. J., & Mueser, K. T. (2007). A meta-analysis of cognitive remediation in schizophrenia. *American Journal of Psychiatry, 164*(12), 1791-1802.
- McGurk, S. R., Mueser, K. T., & Pascaris, A. (2005). Cognitive training and supported employment for persons with severe mental illness: One-year results from a randomized controlled trial. *Schizophrenia Bulletin, 31*(4), 898-909.
- Medalia, A., & Richardson, R. (2005). What predicts a good response to cognitive remediation interventions? *Schizophrenia Bulletin, 31*, 942-953.
- Medalia, A., Revheim, N., & Casey, M. (2001). The remediation of problem-solving skills in schizophrenia. *Schizophrenia Bulletin, 27*, 259-267.
- Medalia, A., Revheim, N., & Herlands, T. (2009). *Cognitive remediation for psychological disorders: Therapist guide (treatments that work)*. Oxford: Oxford University Press.

- Mohamed, S., Rosenheck, R., & Swartz, M. (2008). Relationship of cognition and psychopathology to functional impairment in schizophrenia. *American Journal of Psychiatry*, *165*, 978-987.
- Murthy, N. V., Mahncke, H., Wexler, B. E., Maruff, P., Inamdar, A., & Zucchetto, M. et al. (2012). Computerized cognitive remediation training for schizophrenia: An open label, multi-site, multinational methodology study. *Schizophrenia Research*, *139*(1-3), 87-91.
- 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. *Schizophrenia Research*, *72*(1), 29-39.
- Nuechterlein, K. H., Green, M. F., Kern, R. S., Baade, L. E., Barch, D. M., Cohen, J. D. et al. (2008). *The MATRICS consensus cognitive battery, part 1: Test selection, reliability, and validity*. *The American Journal of Psychiatry* *165*(2), 203-213.
- Poletti, S., Anselmetti, S., Bechi, M., Ermoli, E., Bosia, M., Smeraldi, E. et al. (2010). Computer-aided neurocognitive remediation in schizophrenia: Durability of rehabilitation outcomes in a follow-up study. *Neuropsychological Rehabilitation*, *20*(5), 659-674.
- Rauchensteiner, S., Kawohl, W., Ozgurdal, S., Littmann, E., Gudlowski, Y., Witthaus, H. et al. (2011). Test-performance after cognitive training in persons at risk mental state of schizophrenia and patients with schizophrenia. *Psychiatry Research*, *185*(3), 334-339.

- Sartory, G., Zorn, C., Groetzinger, G. & Windgassen, K. (2005). Computerized cognitive remediation improves verbal learning and processing speed in schizophrenia. *Schizophrenia Research*, 75(2-3), 219-223.
- Twamley, E. W., Doshi, R. R., & Nayak, G. V. (2002). Generalized cognitive impairments, ability to perform everyday tasks, and level of independence in community living situations of older patients with psychosis. *American Journal of Psychiatry*, 159, 2013-2020.
- Vauth, R., Corrigan, P. W., Clauss, M., Dietl, M., Dreher-Rudolph, M., Stieglitz, R. et al. (2005). Cognitive strategies versus self-management skills as adjunct to vocational rehabilitation. *Schizophrenia Bulletin*, 31(1), 55-66.
- Vita, A., De Peri, L., Barlati, S., Cacciani, P., Deste, G., Poli, R. et al. (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. *Schizophrenia Research*, 133(1-3), 223-231.
- Wolwer, W., Frommann, N., Halfmann, S., Piaszek, A., Streit, M., & Gaebel, W. (2005). Remediation of impairments in facial affect recognition in schizophrenia: Efficacy and specificity of a new training program. *Schizophrenia Research*, 80(2-3), 295-303.
- World health Organsiation. *Mental health: Schizophrenia*. Retrieved 4th June, 2012, from http://www.who.int/mental_health/management/schizophrenia/en/

Wykes, T., & Spaulding, W. D. (2011). Thinking about the future cognitive remediation therapy: what works and could we do better? *Schizophrenia Bulletin*, 37(2), 80-90.

All references

- August, S., Kiwanuka, J., McMahon, R. & Gold, J. (2012). The MATRICS consensus cognitive battery (MCCB): Clinical and cognitive correlates. *Schizophrenia Research, 134*(1), 76-82.
- Bark, M., Revheim, N., Huq, F., Kaldherov, V., Ganz, Z.V. & Medalia, A. (2003). The impact of cognitive remediation on psychiatric symptoms in schizophrenia. *Schizophrenia Research, 63* (3), 229–235.
- Barch, D. M. & Keefe, R. S. E. (2010). Anticipating DSM-V: Opportunities and challenges for cognition and psychosis. *Schizophrenia Bulletin, 36*(1), 43-47.
- Bell, M. D. & Bryson, G. (2001). Work rehabilitation in schizophrenia: Does cognitive impairment limit improvement? *Schizophrenia Bulletin, 27*, 269-279.
- Bell, M., Bryson, G., Greig, T., Fiszdon, J. & Wexler, B. E. (2005). Neurocognitive enhancement therapy with work therapy: Productivity outcomes at 6- and 12-month follow-ups. *Journal of Rehabilitation Research and Development, 42*, 829-838.
- Bell, M., Fiszdon, J., Greig, T., Wexler, B. & Bryson, G. (2007). Neurocognitive enhancement therapy with work therapy in schizophrenia: 6-month follow-up of neuropsychological performance. *Journal of Rehabilitation Research and Development 44*, 761–770.
- Bell, M. D., Zito, W., Greig, T. & Wexler, B. E. (2008). Neurocognitive enhancement therapy with vocational services: Work outcomes at two-year follow-up. *Schizophrenia Research, 105*(1-3), 18-29.
- Bellack, A.S., Dickinson, D., Morris, S.E. & Tenhula, W.N. (2005). The

- development of a computer-assisted cognitive remediation program for patients with schizophrenia. *The Israel Journal of Psychiatry and Related Sciences*, 42(1), 5-14.
- Bellack, A. S., Morrison, R. L., Wixted, J. T. & Mueser, K. T. (1990). An analysis of social competence in schizophrenia. *The British Journal of Psychiatry*, 156, 809-819.
- Bellucci, D. M., Glaberman, K. & Haslam, N. (2003). Computer-assisted cognitive rehabilitation reduces negative symptoms in the severely mentally ill. *Schizophrenia Research*, 59(2-3), 225-232.
- Bender, S., Dittmann-Balcar, A., Prehn, G., Thienel, R., Peters, S. & Gastpar, M. (2004). Subjective experience of a computer-assisted cognitive training by patients with schizophrenia. *Nervenarzt*, 75(1), 44-50.
- Benedict, R.H.B., Harris, A.E., Markow, T., McCormick, J.A., Nuechterlein, K.H. & Asarnow, R.F. (1994). Effects of attention training on information processing in schizophrenia. *Schizophrenia Bulletin* 20, 537–546.
- Bilder, R. M., Goldman, R. S., Robinson, D., Reiter, G., Bell, L., Bates, J. A. *et al.* (2000). Neuropsychology of first-episode schizophrenia: Initial characterization and clinical correlates. *American Journal of Psychiatry*, 157(4), 549-559.
- Birchwood, M., Smith, J., Cochrane, R., Wetton, S. & Copestake, S. (1990). The social functioning scale. the development and validation of a new scale of social adjustment for use in family intervention programmes with schizophrenic patients. *The British Journal of Psychiatry*, 157(6), 853-859.
- Bowie, C. R., McGurk, S. R., & Mueser, K. T., Patterson, T.L. & Harvey, P.D. (2012). Combined cognitive remediation and functional skills training for

- schizophrenia: Effects on cognition, functional competence, and real-world behavior. *American Journal of Psychiatry*, 169, 710-718.
- Burda, P.C., Starkey, T.W., Dominguez, F. & Vera, V. (1994). Computer-assisted cognitive rehabilitation of chronic psychiatric inpatients. *Computers in Human Behavior*, 10, 359–368.
- Cassidy, J.J., Easton, M., Capelli, C., Singer, A. & Bilodeau, A. (1996). Cognitive remediation of persons with severe and persistent mental illness. *Psychiatric Quarterly*, 67, 313– 321.
- Cavallaro, R., Anselmetti, S., Poletti, S., Bechi, M., Ermoli, E., Cocchi, F. *et al.* (2009). Computer-aided neurocognitive remediation as an enhancing strategy for schizophrenia rehabilitation. *Psychiatry Research*, 169(3), 191-196.
- Centre for Reviews and Dissemination. (2009). *Systematic reviews: CRD's guidance for undertaking reviews in health care*. The University of York: Retrieved 10 May 2012 from www.york.ac.uk/inst/crd/index_guidance.htm.
- Cogpack (version 8.34). (2012). *Technical manual*. Ladenburg: Marker.
- d'Amato, T., Bation, R., Cochet, A., Jalenques, I., Galland, F., Giraud-Baro, E. *et al.* (2011). A randomized, controlled trial of computer-assisted cognitive remediation for schizophrenia. *Schizophrenia Research*, 125(2-3), 284-290.
- Dickerson, F., Boronow, J. J., Ringel, N. & Parente, F. (1996). Neurocognitive deficits and social functioning in outpatients with schizophrenia. *Schizophrenia Research*, 21(2), 75-83.
- Dickinson, D., Tenhula, W., Morris, S., Brown, C., Peer, J., Spencer, K *et al.* (2010). A randomized, controlled trial of computer-assisted cognitive remediation for schizophrenia. *American Journal of Psychiatry*, 167(2), 170-180.

- Eack, S. M., Greenwald, D. P., Hogarty, S. S., Cooley, S. J., DiBarry, A. L.,
Montrose, D. M. *et al.* (2009). Cognitive enhancement therapy for early-course
schizophrenia: Effects of a two-year randomized controlled trial. *Psychiatric
Services, 60*(11), 1468-1476.
- Eack, S.M., Hogarty, G.E., Greenwald, D.P., Hogarty, S.S. & Keshavan, M.S.
(2007). Cognitive enhancement therapy improves emotional intelligence in
early course schizophrenia : preliminary effects. *Schizophrenia Research 89*,
308–311.
- Eaton, W. W., Thara, R., Federman, B., Melton, B. & Liang, K. (1995). Structure
and course of positive and negative symptoms in schizophrenia. *Archives of
General Psychiatry, 52* (2), 127-134.
- Elvevåg, B., & Goldberg, T. E. (2000). Cognitive impairment in schizophrenia is the
core of the disorder. *Critical Reviews in Neurobiology, 14*(1), 1-21.
- Faul, F., Erdfelder, E., Lang, A. G. & Buchner, A. (2007). G*Power 3: A flexible
statistical power analysis program for the social, behavioral, and biomedical
sciences. *Behavior Research Methods, 39*(2), 175-191.
- Field, A. (2005). *Discovering statistics using SPSS* (2nd ed.). London: SAGE
publications.
- Field, C. D., Galletly, C., Anderson, D. & Walker, P. (1997). Computer-aided
cognitive rehabilitation: Possible application to the attentional deficit of
schizophrenia, a report of negative results. *Perceptual & Motor Skills, 85*(3 Pt
1), 995-1002.

- Fisher, M., Holland, C., Subramaniam, K. & Vinogradov, S. (2010). Neuroplasticity-based cognitive training in schizophrenia: An interim report on the effects 6 months later. *Schizophrenia Bulletin*, 36(4), 869-879.
- Fiszdon, J.M., Bryson, G.J., Wexler, B.E. & Bell, M.D. (2004). Durability of cognitive remediation training in schizophrenia: performance on two memory tasks at 6-month and 12-month follow-up. *Psychiatry Research*, 125, 1-7.
- Fiszdon J.M., Choi, J., Bryson, G.J. & Bell, M.D. (2006). Impact of intellectual status on response to cognitive task training in patients with schizophrenia. *Schizophrenia Research* 87, 261-269.
- Galderisi, S., Piegari, G., Mucci, A., Acerra, A., Luciano, L. & Rabasca, A. F. *et al.* (2010). Social skills and neurocognitive individualized training in schizophrenia: Comparison with structured leisure activities. *European Archives of Psychiatry and Clinical Neuroscience*, 260(4), 305-315.
- Gold, J. M. (2004). Cognitive deficits as treatment targets in schizophrenia. *Schizophrenia Research*, 72(1), 21-28.
- Granholm, E., McQuaid, J. R., McClure, F. S., Auslander, L. A., Perivoliotis, D., Pedrelli, P. *et al.* (2005). A randomized, controlled trial of cognitive behavioral social skills training for middle-aged and older outpatients with chronic schizophrenia *American Journal of Psychiatry*, 162, 520-529.
- Green, M. F. (1996). What are the functional consequences of neurocognitive deficits in schizophrenia? *The American Journal of Psychiatry*, 153(3), 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”? *Schizophrenia Bulletin*, 26(1), 119-136.

- Green, M.F., Nuechterlein, K.H., Kern, R.S., Baade, L.E., Fenton, W.S., Gold, J.M.,
et al. (2008). Functional co-primary measures for clinical trials in schizophrenia:
Results from the MATRICS psychometric and standardization study. *American
Journal of Psychiatry*, *165*, 221-228.
- Greig, T.C., Zito, W., Wexler, B.E., Fiszdon, J. & Bell, M.D. (2007). Improved
cognitive function in schizophrenia after one year of cognitive training and
vocational services. *Schizophrenia Research* *96*, 156–161.
- Grynszpan, O., Perbal, S., Pelissolo, A., Fossati, P., Jouvent, R., Dubal, S. *et al.*
(2011). Efficacy and specificity of computer-assisted cognitive remediation in
schizophrenia: A meta-analytical study. *Psychological Medicine*, *41*(01), 163-
173.
- Heaton, R. K., Gladsjo, J. A., Palmer, B. W., Kuck, J., Marcotte, T. D. & Jeste, D. V.
(2001). Stability and course of neuropsychological deficits in schizophrenia.
Archives of General Psychiatry, *58*, 24-32.
- Hermanutz, M. & Gestrich, J. (1991). Computer-assisted attention training in
schizophrenics: A comparative study. *European Archives of Psychiatry and
Clinical Neuroscience*, *240*(4-5), 282-287.
- Heydebrand, G. (2007) Issues in Rehabilitation of Cognitive Deficits in
Schizophrenia: A Critical Review. *Current Psychiatry Reviews*, *3* (3), 186-195.
- Hodge, M. A., Siciliano, D., Withey, P., Moss, B., Moore, G., & Judd, G. *et al.*
(2010). A randomized controlled trial of cognitive remediation in
schizophrenia. *Schizophrenia Bulletin*, *36*(2), 419-427.
- Hogarty, G. E., Flesher, S., Ulrich, R., Carter, M., Greenwald, D., Pogue-Geile, M. *et al.*
(2004). Cognitive enhancement therapy for schizophrenia: Effects of a 2-

- year randomized trial on cognition and behavior. *Archives of General Psychiatry*, 61(9), 866-876.
- Hogarty, G.E, Greenwald, D.P. & Eack, S.M. (2006). Durability and Mechanism of Effects of Cognitive Enhancement Therapy. *Psychiatric Services*, 57 (12), 1751, 1757.
- Hunter, R. & Barry, S. (2011). Negative symptoms and psychosocial functioning in schizophrenia: neglected but important targets for treatment. *European Psychiatry*, 27 (6), 432-436.
- Keefe, R. S., Poe, M., Walker, T. M. & Harvey, P. D. (2006). The relationship of the brief assessment of cognition in schizophrenia (BACS) to functional capacity and real-world functional outcome. *Journal of Clinical and Experimental Neuropsychology*, 28(2), 260-269.
- Keefe, R. S. E., Vinogradov, S., Medalia, A., Silverstein, S. M., Bell, M. D., Dickinson, D. *et al.* (2011). Report from the working group conference on multisite trial design for cognitive remediation in schizophrenia. *Schizophrenia Bulletin*, 37(5), 1057-1065.
- Krabbendam, L. & Aleman, A. (2003). Cognitive rehabilitation in schizophrenia: A quantitative analysis of controlled studies. *Psychopharmacology*, 169, 376-382.
- Kurtz, M. M., Moberg, P. J., Gur, R. C. & Gur, R. E. (2001). Approaches to cognitive remediation of neuropsychological deficits in schizophrenia: A review and meta-analysis. *Neuropsychology Review*, 11(4), 197-210.
- 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? *Schizophrenia Research* 89, 251–260.

- Kurtz, M.M., Seltzer, J.C., Fujimoto, M., Shagan, D.S. & Wexler, B.E. (2009). Predictors of change in life skills in schizophrenia after cognitive remediation. *Schizophrenia Research*, 107 (2-3), 267-274.
- Kurtz, M.M., Wexler, B.E., Fujimoto, M., Shagan, D.S. & Seltzer, J.C. (2008). Symptoms versus neurocognition as predictors of change in life skills in schizophrenia after outpatient rehabilitation. *Schizophrenia Research*, 102 (1-3), 303-311.
- Lecardeur, L., Stip, E., Giguere, M., Blouin, G., Rodriguez, J.P. & Champagne-Lavau, M. (2009). Effects of cognitive remediation therapies on psychotic symptoms and cognitive complaints in patients with schizophrenia and related disorders: a randomized study. *Schizophrenia Research*, 111(1-3):153-8.
- Leifker, F. R., Patterson, T. L., Bowie, C. R., Mausbach, B. T. & Harvey, P. D. (2010). Psychometric properties of performance-based measurements of functional capacity: Test–retest reliability, practice effects, and potential sensitivity to change. *Schizophrenia Research*, 119(1-3), 246-252.
- Leifker, F. R., Patterson, T. L., Heaton, R. K. & Harvey, P. D. (2011). Validating measures of real-world outcome: The results of the VALERO expert survey and RAND panel *Schizophrenia Bulletin*, 37(2), 334-343.
- Lewis, L., Unkefer, E.P., O’Neal, S.K., Crith, C.J. & Fultz, J. (2003). Cognitive rehabilitation with patients having persistent, severe psychiatric disabilities. *Psychiatric Rehabilitation*, 26, 325–331.
- Lindenmayer, J., McGurk, S. R., Mueser, K. T., Khan, A., Wance, D., Hoffman, L. *et al.* (2008). A randomized controlled trial of cognitive remediation among inpatients with persistent mental illness. *Psychiatric Services*, 59(3), 241-247.

- López-Luengo, B. & Vázquez, C. (2003). Effects of Attention Process Training on cognitive functioning of schizophrenic patients. *Psychiatry Research*, 119(1-2), 41-53.
- Mangalore, R. & Knapp, M. (2007). Cost of schizophrenia in England. *The Journal of Mental Health Policy and Economics*, 10(1), 23-41.
- Mausbach, B. T., Moore, R., Bowie, C., Cardenas, V. & Patterson, T. L. (2009). A review of instruments for measuring functional recovery in those diagnosed with psychosis. *Schizophrenia Bulletin*, 35(2), 307-318.
- Mausbach, B. T., Harvey, P. D., Goldman, S. R., Jeste, D. V. & Patterson, T. L. (2007). Development of a brief scale of everyday functioning in persons with serious mental illness. *Schizophrenia Bulletin*, 33(6), 1364-1372.
- McGurk, S. R., Mueser, K. T., DeRosa, T. J. & Wolfe, R. (2009). Work, recovery, and comorbidity in schizophrenia: A randomized controlled trial of cognitive remediation. *Schizophrenia Bulletin*, 35(2), 319-335.
- McGurk, S. R., Mueser, K. T. & Pascaris, A. (2005). *Cognitive training and supported employment for persons with severe mental illness: One-year results from a randomized controlled trial*. *Schizophrenia Bulletin*, 31(4), 898-909.
- McGurk, S. R., Twamley, E. W., Sitzer, D. I., McHugo, G. J. & Mueser, K. T. (2007). A meta-analysis of cognitive remediation in schizophrenia. *American Journal of Psychiatry*, 164(12), 1791-1802.
- Medalia, A., Aluma, M., Tryon, W. & Merriam, A. E. (1998). Effectiveness of attention training in schizophrenia. *Schizophrenia Bulletin*, 24(1), 147-152.
- Medalia, A. & Choi, J., 2009. Cognitive remediation in schizophrenia. *Neuropsychology Review*, 19 (3), 353–364.
- Medalia, A., Revheim, N., Casey, M. (2000). Remediation of memory disorders in

- schizophrenia. *Psychological Medicine* 30, 1451–1459.
- Medalia, A., Revheim, N. & Casey, M. (2001). The remediation of problem-solving skills in schizophrenia. *Schizophrenia Bulletin*, 27, 259-267.
- Medalia, A., Revheim, N. & Casey, M. (2002). Remediation of problem-solving skills in schizophrenia : evidence of a persistent effect. *Schizophrenia Research* 57, 165–171.
- Medalia, A., Revheim, N & Herlands, T. (2009). *Cognitive remediation for psychological disorders: Therapist guide (treatments that work)*. Oxford: Oxford University Press.
- Medalia, A. & Richardson, R. (2005). What predicts a good response to cognitive remediation interventions? *Schizophrenia Bulletin*, 31, 942-953.
- Mohamed, S., Rosenheck, R., & Swartz, M. (2008). Relationship of cognition and psychopathology to functional impairment in schizophrenia. *American Journal of Psychiatry*, 165, 978-987.
- Morris, S. (2008). Estimating effect sizes from pretest-posttest-control group designs. *Organizational Research Methods*, 11(2), 364-386.
- Murthy, N. V., Mahncke, H., Wexler, B. E., Maruff, P., Inamdar, A., Zucchetto, M. et al. (2012). Computerized cognitive remediation training for schizophrenia: An open label, multi-site, multinational methodology study. *Schizophrenia Research*, 139(1–3), 87-91.
- 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. *Schizophrenia Research*, 72(1), 29-39.

- Nuechterlein, K. H. & Green, M. F. (2006). *Matrics consensus cognitive battery: Manual*. MATRICS Assessment Inc.
- Nuechterlein, K. H., Green, M. F., Kern, R. S., Baade, L. E., Barch, D. M., Cohen, J. D. *et al.* (2008). The MATRICS consensus cognitive battery, part 1: Test selection, reliability, and validity. *The American Journal of Psychiatry*, *165*(2), 203-213.
- Olbrich, R. & Mussgay, L. (1990). Reduction of schizophrenic deficits by cognitive training: an evaluative study. *European Archives of Psychiatry and Neurological Sciences*, *239*, 366–369.
- Patterson, T. L., Goldman, S., McKibbin, C. L., Hughs, T. & Jeste, D. V. (2001). UCSD performance-based skills assessment: Development of a new measure of everyday functioning for severely mentally ill adults. *Schizophrenia Bulletin*, *27*(2), 235-245.
- Patterson, T. L., Mausbach, B. T., McKibbin, C., Goldman, S., Bucardo, J. & Jeste, D. V. (2006). Functional adaptation skills training (FAST): A randomized trial of a psychosocial intervention for middle-aged and older patients with chronic psychotic disorders. *Schizophrenia Research*, *86*(1–3), 291-299.
- Pilling, S., Bebbington, P., Kuipers, E., Garety, P., Geddes, J., Martindale, B. *et al.* (2002). Psychological treatments in schizophrenia: II. meta-analyses of randomized controlled trials of social skills training and cognitive remediation. *Psychological Medicine*, *32*, 783-791.
- Poletti, S., Anselmetti, S., Bechi, M., Ermoli, E., Bosia, M., Smeraldi, E. *et al.* (2010). Computer-aided neurocognitive remediation in schizophrenia:

- Durability of rehabilitation outcomes in a follow-up study. *Neuropsychological Rehabilitation*, 20(5), 659-674.
- Rauchensteiner, S., Kawohl, W., Ozgurdal, S., Littmann, E., Gudlowski, Y., Witthaus, H. *et al.* (2011). Test-performance after cognitive training in persons at risk mental state of schizophrenia and patients with schizophrenia. *Psychiatry Research*, 185(3), 334-339.
- Roder, V., Mueller, D.R., Mueser, K.T. & Brenner, H.D. (2006). Integrated psychological therapy (IPT) for schizophrenia: is it effective? *Schizophrenia Bulletin*, 32 (Suppl. 1), S81–S93.
- Sartory, G., Zorn, C., Groetzinger, G. & Windgassen, K. (2005). Computerized cognitive remediation improves verbal learning and processing speed in schizophrenia. *Schizophrenia Research*, 75(2-3), 219-223.
- Scottish Intercollegiate Guidelines Network (SIGN) guideline. (2009). *Schizophrenia: Core interventions in the treatment and management of schizophrenia in adults in primary and secondary care*. Edinburgh, UK.
- Spaulding, W.D., Fleming, S.K., Reed, D., Sullivan, M., Storzbach, D. & Lam, M. (1999). Cognitive functioning in schizophrenia: Implications for psychiatric rehabilitation. *Schizophrenia Bulletin*, 25(2), 275-289.
- Surti, T.S., Corbera, S., Bell, M.D. & Wexler, B.E. (2011). Successful computer-based visual training specifically predicts visual memory enhancement over verbal memory improvement in schizophrenia. *Schizophrenia Research*, 132(2-3), 131-134.
- Twamley, E. W., Doshi, R. R., Nayak, G. V., Palmer, B.W., Golshan, S., Heaton, R.K. *et al.* (2002). Generalized cognitive impairments, ability to perform

everyday tasks, and level of independence in community living situations of older patients with psychosis. *American Journal of Psychiatry*, 159(12), 2013-2020.

Twamley, E.W., Jeste, D.V. & Bellack, A.S. (2003). A review of cognitive training in schizophrenia. *Schizophrenia Bulletin*, 29(2), 359-382.

Vauth, R., Corrigan, P. W., Clauss, M., Dietl, M., Dreher-Rudolph, M., Stieglitz, R. *et al.* (2005). Cognitive strategies versus self-management skills as adjunct to vocational rehabilitation. *Schizophrenia Bulletin*, 31(1), 55-66.

Vesterager, L. Christensen, T. Olsen, B.B., Krarup, G., Forchhammer, H., Melau, M. (2011). Cognitive training plus a comprehensive psychosocial programme (OPUS) versus the comprehensive psychosocial programme alone for patients with first-episode schizophrenia (the NEUROCOM trial): A study protocol for a centrally randomised, observer-blinded multi-centre clinical trial. *Trials*, 12, 35-

Vita, A., De Peri, L., Barlati, S., Cacciani, P., Deste, G., Poli, R. *et al.* (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. *Schizophrenia Research*, 133(1-3), 223-231.

Wolwer, W., Frommann, N., Halfmann, S., Piaszek, A., Streit, M. & Gaebel, W.

(2005). Remediation of impairments in facial affect recognition in schizophrenia: Efficacy and specificity of a new training program.

Schizophrenia Research, 80(2-3), 295-303.

World Health Organisation (2012). *Mental health: Schizophrenia*. Available at:
http://www.who.int/mental_health/management/schizophrenia/en/. Retrieved 4
June 2012.

Wykes, T. & Spaulding, W. D. (2011). Thinking about the future cognitive
remediation Therapy. What works and could we do better? *Schizophrenia
Bulletin*, 37(suppl 2), S80-S90.

Appendixes

Appendix 1: Author Guidelines

The Editorial Board of the British Journal of Psychology is prepared to consider for publication:

- (a) reports of empirical studies likely to further our understanding of psychology
- (b) critical reviews of the literature
- (c) theoretical contributions Papers will be evaluated by the Editorial Board and referees in terms of scientific merit, readability, and interest to a general readership.

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The circulation of the Journal is worldwide. Papers are invited and encouraged from authors throughout the world.

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Appendix 2. Quality criteria scoring guidelines

1.1) The study addresses an appropriate and clearly focused question.	
Well-covered (2)	A clear description of an appropriate focused question is provided.
Adequately addressed (1)	A description of a focused question is provided
Poorly addressed (0)	It is not clear what the focused question is or there may be multiply questions.
Not addressed (0)	There is no description of a focused question
Not reported (0)	A question mentioned but insufficient detail provided
Not applicable (0)	

1.2) The assignment of subjects to treatment groups is randomised.	
Well-covered (2)	Randomisation is clearly described and an appropriate method was used.
Adequately addressed (1)	Randomisation is carried out but no description of method given.
Poorly addressed (0)	Randomisation is carried out through the use of inappropriate method (alternate allocation, allocation by date of birth, or day of the week attending a clinic).
Not addressed (0)	Randomisation was not carried out or described.
Not reported (0)	Insufficient information given to assess randomization process.
Not applicable (0)	

1.3) An adequate concealment method is used.	
Well-covered (2)	Concealment is clearly described and an appropriate method was used to ensure researcher unaware of subject group allocation at the time they enter the study.
Adequately addressed (1)	Concealment is carried out to ensure researcher unaware of subject group allocation at the time they enter the study but no description of method given.
Poorly addressed (0)	Concealment was partially carried out (e.g. some researchers unaware of subject group allocation at the time they entered the study).
Not addressed (0)	No methods of concealment used.
Not reported (0)	Insufficient information given to assess concealment.
Not applicable (0)	

1.4) Subjects and investigators are kept 'blind' about treatment allocation.	
Well-covered (2)	Both the patient and researcher conducting the outcome assessments are blind to conditions and a detailed description of method given.
Adequately addressed (1)	The researcher conducting the outcome assessments are blind to conditions but description not given.
Poorly addressed (0)	Blinding is carried out through the use of inappropriate method or was partially carried out.
Not addressed (0)	No blinding procedures carried out or described.
Not reported (0)	Insufficient information given to assess blinding.
Not applicable (0)	

1.5) The treatment and control groups are similar at the start of the trial.	
Well-covered (2)	Clear details of baseline characteristics between groups. No difference between groups or differences controlled for.
Adequately addressed (1)	Reasonable detail of baseline characteristics between groups, and reasonably similar at baseline.
Poorly addressed (0)	Baseline characteristics assessed but limited description provided or groups different at baseline and not controlled for.
Not addressed (0)	Baseline characteristics not assessed or not reported.
Not reported (0)	Insufficient information given to assess whether treatment was only difference.
Not applicable (0)	

1.6) The only difference between groups is the treatment under investigation.	
Well-covered (2)	Detailed consideration has been to this point and it is clear that the treatment is the only difference between groups.
Adequately addressed (1)	Some consideration has been to this point and it is likely that the treatment is the only difference between groups.
Poorly addressed (0)	Consideration has been given to this point but limited description given and it is unclear whether the treatment was the only difference between groups.
Not addressed (0)	No consideration has been given to this point
Not reported (0)	Insufficient information given to assess whether treatment was only difference.
Not applicable (0)	

1.7). All relevant outcomes are measured in a standard, valid and reliable way.	
Well-covered (2)	Outcome measures clearly described and acceptable/good robustness for use with individuals with schizophrenia.
Adequately addressed (1)	Outcome measures acceptable/good robustness but not designed for use with individuals with schizophrenia.
Poorly addressed (0)	Outcome measures poorly described and less robust.
Not addressed (0)	Outcome measures used were not robust (not standardised in any way)
Not reported (0)	Insufficient information given to assess whether measures were robust.
Not applicable (0)	

1.8) What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out?	
Well-covered (2)	A detailed description of the number of drop outs in each treatment arm was given and consideration to the reasons for this.
Adequately addressed (1)	A description of the number of drop outs in each treatment arm was given.
Poorly addressed (0)	No description of drop outs given but numbers can be identified from tables etc.
Not addressed (0)	No description of drop outs given.
Not reported (0)	Insufficient information given to assess what percentage of individuals in each treatment arm dropped out.
Not applicable (0)	

1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).	
Well-covered (2)	Intention-to-treat analyses are well described and all subjects analysed in their appropriate group.
Adequately addressed (1)	Intention-to-treat analyses was mentioned but not described in any detail.
Poorly addressed (0)	It was not clear if intention-to-treat analyses was used.
Not addressed (0)	No intention-to-treat analysis was used
Not reported (0)	Insufficient information given to assess whether intention-to-treat analyses was used.
Not applicable (0)	

1.10) Where the study is carried out at more than one site, results are comparable for all sites	
Well-covered (2)	A detailed description of the results from each site is provided and consideration is given as to whether the results are comparable.
Adequately addressed (1)	Some description of the results from each site is provided and consideration is given as to whether the results are comparable.
Poorly addressed (0)	description of the results from each site is provided and consideration is given as to whether the results are comparable
Not addressed (0)	No description of the results from each site is provided and no consideration is given as to whether the results are comparable.
Not reported (0)	Insufficient information given to assess whether the results are comparable across sites.
Not applicable (0)	

Appendix 3. Studies excluded from the review.

Authors	Reason for exclusion
Fiszdon <i>et al.</i> (2004)	Data not available
Fisher (2010)	Duplicate data (Fisher 2009)
Hogarty (2006)	Duplicate data (Hogarty, 2004)
Lindenmayor et al (2008)	Mixed population
McGurk et al (2009)	Mixed population
Kurtz <i>et al.</i> (2009)	No control group
Rauchensteiner <i>et al.</i> (2011)	No control group
Rudnick <i>et al.</i> (2009)	No control group
Surti <i>et al.</i> (2011)	No control group
Benedict <i>et al.</i> .(1994)	No post symptoms assessment
Kurtz <i>et al.</i> (2008)	No post symptoms assessment
McGurk (2007)	No post symptoms assessment
Fiszdon (2006)	Not CACR
Luengo (2003)	Not CACR
Olbrich (1990)	Not CACR
Spaulding (1999)	Not CACR
Lecardeur (2009)	Not CACR
Lewis (2003)	Not CACR
Bark (2003)	Not randomised
Heydebrand <i>et al.</i> (2007)	Review paper
Medalia (2009)	Review paper
Roder (2006)	Review paper
Vesterager <i>et al.</i> (2011)	Study protocol
Bell <i>et al.</i> (2005)	Symptoms not assessed
Bell <i>et al.</i> (2007)	Symptoms not assessed
Bell <i>et al.</i> (2008)	Symptoms not assessed
Bellack <i>et al.</i> (2005)	Symptoms not assessed
Burda <i>et al.</i> (1994)	Symptoms not assessed
Cassidy (1996)	Symptoms not assessed
Eack (2007)	Symptoms not assessed
Greig <i>et al.</i> (2007)	Symptoms not assessed
Kurtz <i>et al.</i> (2007)	Symptoms not assessed
Medalia (2000)	Symptoms not assessed
Medalia (2001)	Symptoms not assessed
Medalia (2002)	Symptoms not assessed
Sartory <i>et al.</i> (2005)	Symptoms not assessed
Cooper <i>et al.</i> (1999)	Symptoms not assessed
Field <i>et al.</i> (1997)	Symptoms not assessed
Pilrac <i>et al.</i> (2000)	Symptoms not assessed

Appendix 4: Participant letter of invitation.



Psychiatric Rehabilitation Department
First Floor
MacLeod
Old Admin Block
Royal Cornhill Hospital
Aberdeen
AB25 2ZH

Date:
Enquiries to: Joanne
Telephone: 01224 557474
Email: joanne.macleod1@nhs.net

Dear Participant

Your clinician has given you this letter of invitation to inform you of a research project that you may be interested in taking part in.

Mental health conditions can often affect a person's memory and cognitive skills. You are being invited to take part in a research project that is investigating a treatment that can improve memory and cognitive skills in individuals with mental health conditions.

I have enclosed a participant information sheet which will explain the project in more detail. If you are willing to participate in the project or would like further information please contact me on 01224 557474. Alternatively, you can ask your clinician to pass you name and contact number to me and I will contact you to discuss the project further.

With many thanks for taking the time to read this letter

I look forward to hearing from you

Joanne MacLeod
Trainee Clinical Psychologist

Cognitive remediation in schizophrenia: version 2

26/08/2011

Consent ID number:

Appendix 5: Participant Information Sheet.



Participant Information Sheet

Project Title: Cognitive remediation in schizophrenia

You are being invited to participate in a research study. Before you decide whether to participate, it is important for you to understand why the research is being done and what it will involve. *One of our team will go through the information sheet with you and answer any questions you have.* We would like to stress that you do not have to accept this invitation and should only agree to take part if you want to.

Project Aims & Objectives

If you have a mental health condition your memory and cognitive skills can often be affected. The aim of this research study is to evaluate a treatment that aims to improve memory and cognitive skills in people with a mental health condition. The study will also investigate whether the treatment can improve daily living skills.

Why have I been chosen to take part?

Individuals who have a diagnosis such as schizophrenia are being invited to take part in this study.

Do I have to take part?

Participation in the research project is voluntary, and you can withdraw from the study at any time. Refusal to take part in the research project will not impact on your ongoing care from NHS Grampian.

What will happen if I take part?

If you decide to take part, you will be asked to attend the psychiatric rehabilitation department for 50 minutes, twice a week over a five week period. During this time you will be asked to complete some tasks on a computer, but you do not need to have good computer skills to take part in the project. You will also be asked to meet with the researcher on four occasions to complete a number of paper and pencil tasks that will be used to investigate whether the treatment has improved your cognitive skills.

Are there any risks in taking part?

There are no known physical or mental risks associated with this type of research.

Are there any benefits in taking part?

There are a number of benefits to taking part in the research project. Participants will take part in a treatment program that has been shown to improve cognitive skills such as memory, concentration and problem solving. The findings of this study will also be used to inform and improve treatment for patients with mental health conditions in the future.

Ethical Approval

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and approved by the North of Scotland Research Ethics Committee.

Will my participation be kept confidential?

All information collected during the project is completely confidential and only the researcher has access to this information. Your GP will be informed of your participation in the study.

What will happen to the results of the study?

This research is being carried out as part of a Doctorate in Clinical Psychology and will be written up as a thesis and submitted to the University of Edinburgh. All participants will be offered the opportunity to have individual feedback of their personal results. The results of this research project may be published at a future date in an academic journal. No one participating in the study will be identifiable in any resulting publications.

What will happen if I want to stop taking part?

You may withdraw from the research project at any time without having to give a reason. If you decide to withdraw, you can request that any data collected will not be used as part of the research project.

Who can I contact if I have further questions?

If you have any questions or would like further information about the project contact:

Joanne MacLeod, Trainee Clinical Psychologist
Psychiatric Rehabilitation Department, First Floor, Old Admin Block, Royal Cornhill Hospital, Aberdeen.
Telephone: 01224 557474

Thank you for taking the time to read this information.

Cognitive remediation in schizophrenia: version 2

25/10/2011

Consent ID number:

Appendix 6: Participant Consent Form.



Participant Consent Form

Study Title: Cognitive remediation in schizophrenia

Researcher: Joanne MacLeod, Trainee Clinical Psychologist

In order to participate in this research project, it is necessary that you give your informed consent. By signing this informed consent form you are indicating that you understand the nature of the study and that you agree to participate in the research. Please consider the following points before signing:

1. I have read and understood the participant information sheet and have been given the opportunity to ask questions about the research project.
2. I understand that my identity will not be linked with my data, and that all information I provide will remain confidential.
3. I agree to my GP being informed about my participation in the research project.
4. I understand that participation in research is voluntary, and that, after any individual research project has begun, I may withdraw from the project at any time.

By signing this form I am stating that I am over 18 years of age, and that I understand the above information and consent to participate in this study being conducted.

Participant Name: _____ **Date:** _____ **Signature:** _____

Researcher Name: _____ **Date:** _____ **Signature:** _____

Researcher's contact details: Joanne MacLeod, Trainee Clinical Psychologist
Psychiatric Rehabilitation Department, First Floor, Old Admin Block, Royal Cornhill Hospital,
Aberdeen. Telephone: 01224 557474

When completed: 1 for participant; 1 for researcher site file; 1 (original) to be kept in medical notes.

Cognitive remediation in schizophrenia: version 1
18/07/2011 Consent ID number:

Appendix 7: Letter to GPs informing of patient participation.



Psychiatric Rehabilitation Department
First Floor
Old Admin Block
Royal Cornhill Hospital
Aberdeen
AB25 2ZH

Date:
Enquiries to: Joanne MacLeod
Telephone: 01224 557474
Email: joanne.macleod1@nhs.net

Dear Dr <<<insert GP name>>>

I am writing to inform you that <<<insert patient name>>> is taking part in a research project investigating the benefits of cognitive remediation in schizophrenia.

During this project cognitive functioning and performance based functioning will be assessed before and after a five week computer intervention program that aims to improve cognitive functioning. In addition to this, all participants will be followed up one-month after the intervention to investigate whether any improvements are maintained.

This project has been approved by the North of Scotland Ethics Committee. If you would like to discuss the project further please do not hesitate to contact me on 01224 557474.

Yours sincerely

Joanne MacLeod
Trainee Clinical Psychologist

Appendix 8: Letter confirming Ethical Approval

NRES Committees - North of Scotland

Summerfield House
2 Eday Road
Aberdeen
AB15 6RE

Telephone: 01224 558474
Facsimile: 01224 558609
Email: nosres@nhs.net



2 September 2011

Miss Joanne MacLeod
Trainee Clinical Psychologist
NHS Grampian
Psychiatric Rehabilitation
First Floor Old Admin Block
Royal Cornhill Hospital
ABERDEEN
AB25 2ZH

Dear Miss MacLeod

Study title: Cognitive remediation in schizophrenia: effects on cognitive functioning and performance based functioning.
REC reference: 11/NS/0012

Thank you for your letter of 27 August 2011, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information was considered by the Ethics Co-ordinator and Scientific Officer.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at <http://www.rdforum.nhs.uk>.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

<i>Document</i>	<i>Version</i>	<i>Date</i>
Covering Letter		27 August 2011
Evidence of insurance or indemnity		18 July 2011
Investigator CV		18 July 2011
Letter of invitation to participant	2	26 August 2011
Other: Supervisor C.V.		21 July 2011
Other: Letter to G.P.	1	18 July 2011
Other: Poster	1	2 September 2011
Participant Consent Form	1	18 July 2011
Participant Information Sheet	2	26 August 2011
Protocol	1	18 July 2011
REC application	3.1	18 July 2011
Referees or other scientific critique report		22 June 2011
Response to Request for Further Information		27 August 2011

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "*After ethical review – guidance for researchers*" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review.

11/NS/0012

Please quote this number on all correspondence

With the Committee's best wishes for the success of this project

Yours sincerely

Cass Irvie

PP

**Dr Ruth Stephenson
Chair**

Enclosures: "After ethical review – guidance for researchers" SL-AR2

Copy to: Miss Gemma Watson, University of Edinburgh
NHSG R&D Department

Appendix 9: Letter confirming R&D approval

Research and Development

Foresterhill House Annexe
Foresterhill
Aberdeen
AB25 2ZB



Miss Joanne MacLeod
Dept of Psychiatric Rehabilitation
NHS Grampian
1st Floor, Old Admin Block
Royal Cornhill Hospital
Aberdeen
AB25 2ZH

Date 26/10/2011
Your Ref 11/NS/0012
Our Ref 2011MH006

Enquiries to
Extension 51121
Direct Line 01224 551121

Dear Miss MacLeod

Management Permission for Non-Commercial Research

MREC Ref: N/A
NOSRES Ref: 11/NS/0012
NRS Ref: N/A
Project title: **Cognitive remediation in schizophrenia: effects on cognitive functioning and performance based functioning.**

Thank you very much for sending all relevant documentation. I am pleased to confirm that the project is now registered with the NHS Grampian Research & Development Office. The project now has R & D Management Permission to proceed locally. This is based on the documents received from yourself and the relevant Approvals being in place.

All research with an NHS element is subject to the Research Governance Framework for Health and Community Care (2006, 2nd edition), and as Chief or Principal Investigator you should be fully committed to your responsibilities associated with this.

It is particularly important that you inform us when the study terminates.

The R&D Office must be notified immediately and any relevant documents forwarded to us if any of the following occur:

- A change of Principal Investigator, Chief Investigator or any additional research personnel
- Premature project termination
- Any amendments – substantial or non-substantial (particularly a study extension)
- Any change to funding or any additional funding

We hope the project goes well, and if you need any help or advice relating to your R&D Management Permission, please do not hesitate to contact the office.

Yours sincerely

A handwritten signature in black ink, appearing to read 'S. Ridge', with a stylized flourish at the end.

Susan Ridge
Non-Commercial Manager

Appendix 10: Tests of Normality

Time 1

Variable	Skewness	Std. Error	Z	Kurtosis	Std. Error	Z
MCCB						
Speed of processing	0.100	0.434	0.230	0.096	0.845	0.114
Attention/vigilance	-0.272	0.434	-0.627	-0.675	0.845	-0.799
Working memory	-0.308	0.434	-0.710	-0.489	0.845	-0.579
Visual learning	0.375	0.434	0.864	-1.042	0.845	-1.233
Verbal learning	0.328	0.434	0.756	-0.814	0.845	-0.963
Reasoning/problem solving	1.023	0.434	2.357	0.919	0.845	1.088
Social cognition	0.364	0.434	0.839	-0.887	0.845	-1.050
UPSA						
Total score	-0.227	0.441	-0.516	-0.834	0.858	-0.971
Social Functioning Scale						
SFS W	0.774	0.434	1.783	1.347	0.845	1.594
SFS IP	-1.163	0.434	-2.680	1.220	0.845	1.444
SFS IC	-0.026	0.434	-0.060	0.069	0.845	0.082

Time 2

Variable	Skewness	Std. Error	Z	Kurtosis	Std. Error	Z
MCCB						
Speed of processing	-0.725	0.472	-1.535	0.597	0.918	0.650
Attention/vigilance	-0.524	0.491	-1.066	-0.660	0.953	-0.693
Working memory	-0.517	0.472	-1.094	-0.373	0.918	-0.407
Visual learning	0.652	0.472	1.380	-0.462	0.918	-0.503
Verbal learning	0.809	0.472	1.713	0.063	0.918	0.069
Reasoning/problem solving	0.283	0.472	0.600	-1.030	0.918	-1.122
Social cognition	0.213	0.472	0.452	-0.169	0.918	-0.184
UPSA-BRIEF						
Total score	-0.031	0.464	-0.067	-1.053	0.902	-1.167
Social Functioning Scale						
SFS W	0.155	0.464	0.334	0.082	0.902	0.091
SFS IP	-1.562	0.464	-3.368	1.836	0.902	2.036
SFS IC	-0.015	0.464	-0.032	-1.162	0.902	-1.289

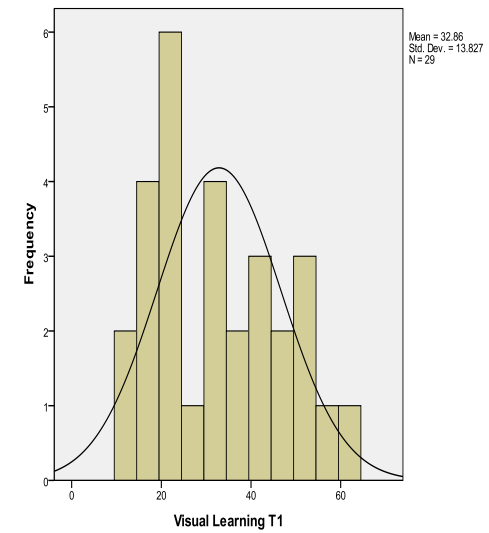
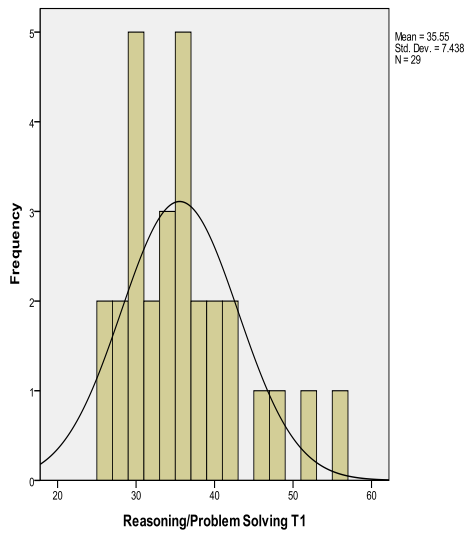
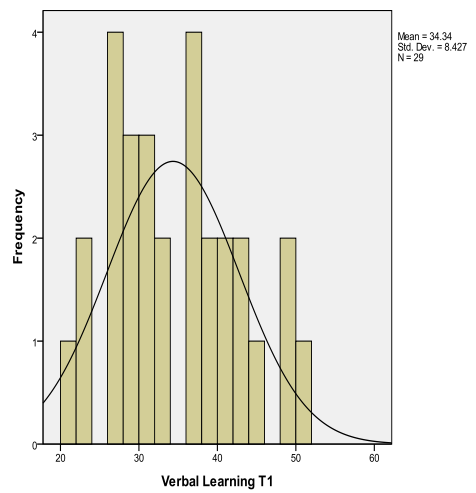
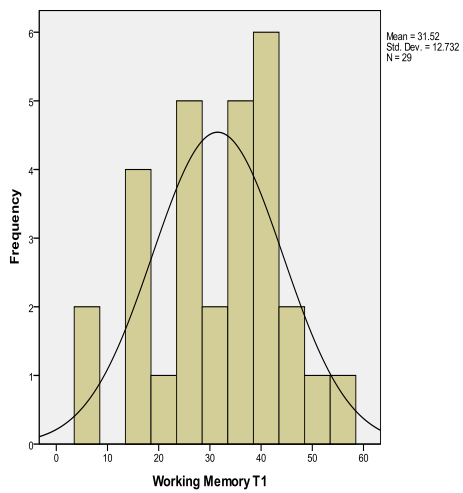
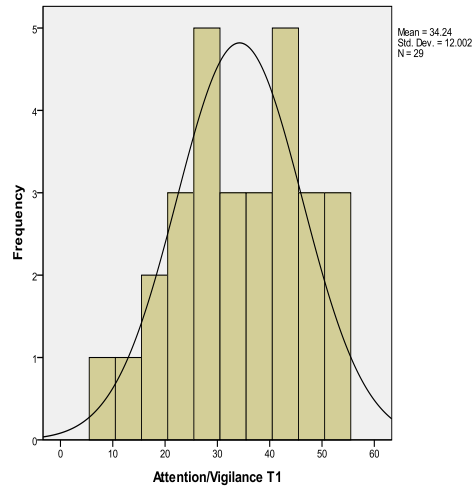
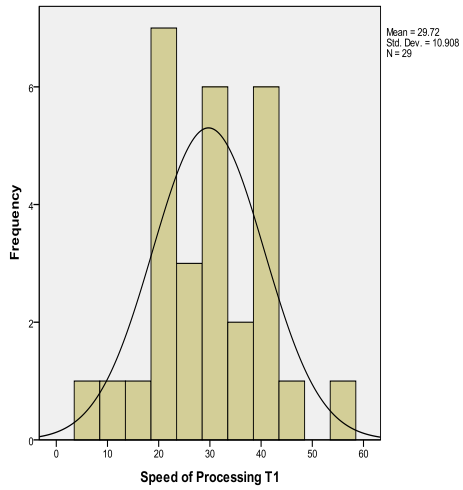
Time 3

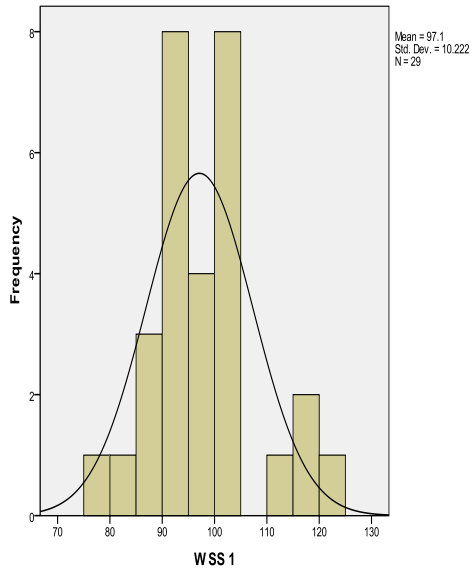
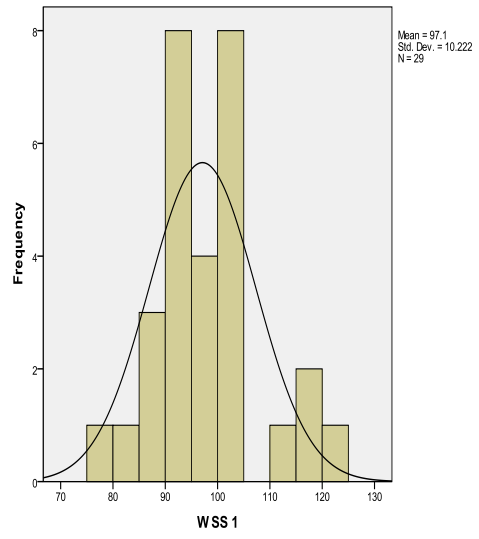
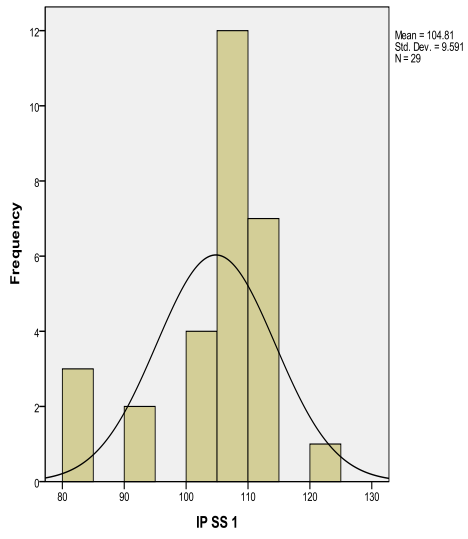
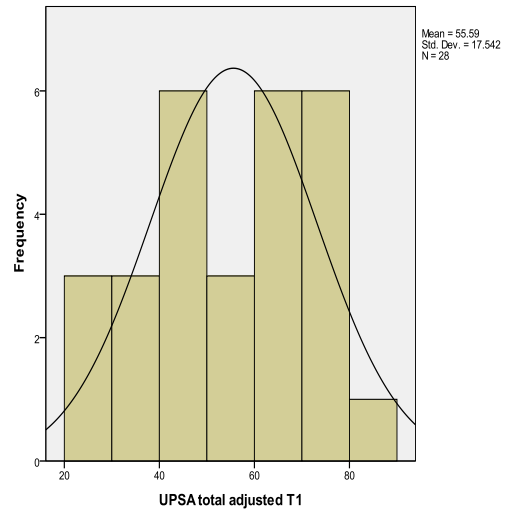
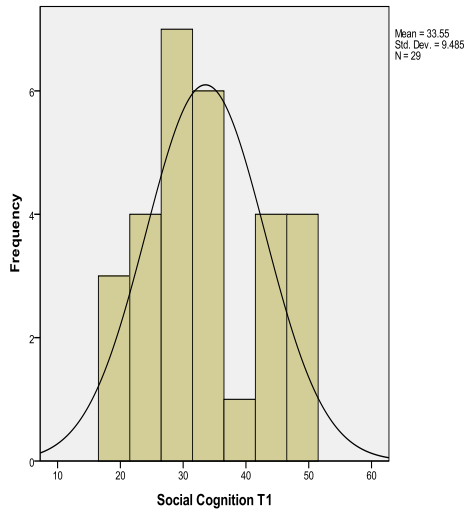
Variable	Skewness	Std. Error	Z	Kurtosis	Std. Error	Z
MCCB						
Speed of processing	-.136	.491	-0.278	.098	.953	0.102
Attention/vigilance	-.203	.491	-0.414	.226	.953	0.237
Working memory	-.982	.491	-1.999	.172	.953	0.181
Visual learning	.581	.501	1.159	-.693	.972	-0.712
Verbal learning	.094	.491	0.191	-.646	.953	-0.678
Reasonong/problem solving	.118	.491	0.240	-1.009	.953	-1.059
Social cognition	-.346	.501	-0.691	-.335	.972	-0.345
UPSA						
Total score	-.552	.491	-1.124	-.548	.953	-0.575
Social Functioning Scale						
SFS W	.155	.464	0.334	.082	.902	0.091
SFS IP	-1.562	.464	-3.368	1.836	1.836	1.000
SFS IC	-.015	.464	-0.032	-1.162	.902	-1.289

Time 4

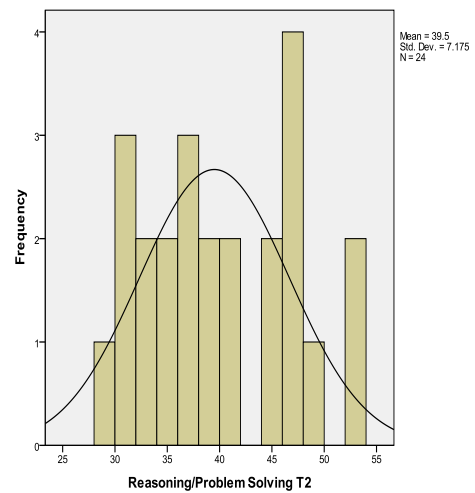
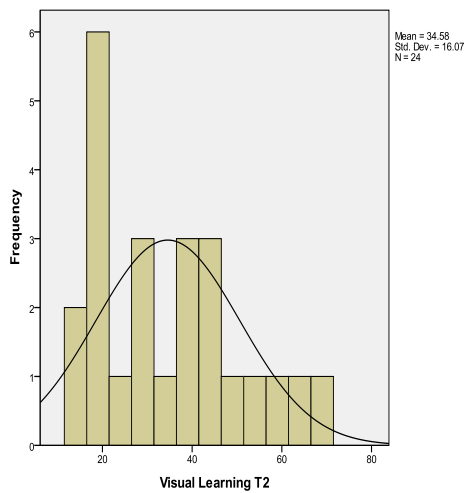
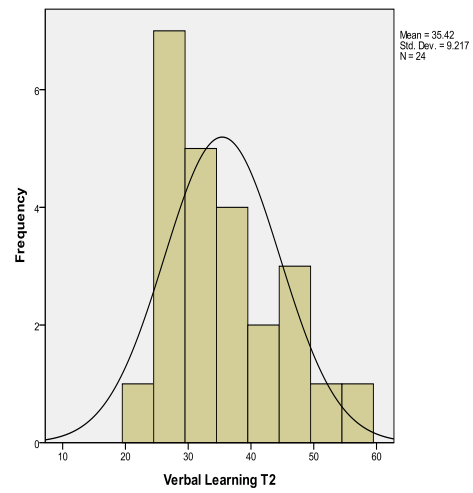
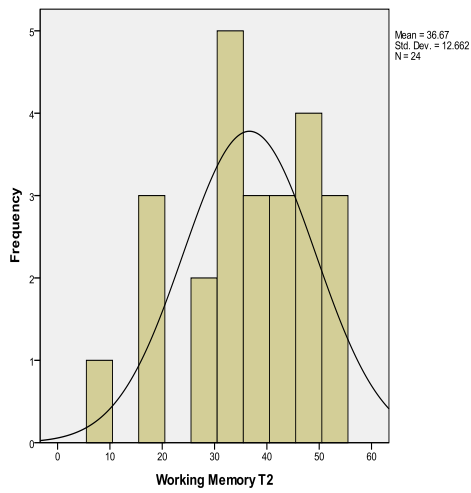
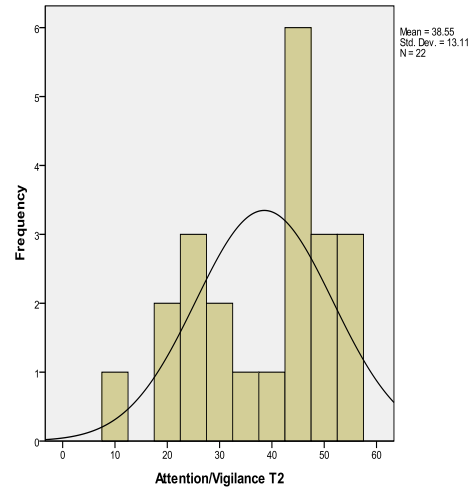
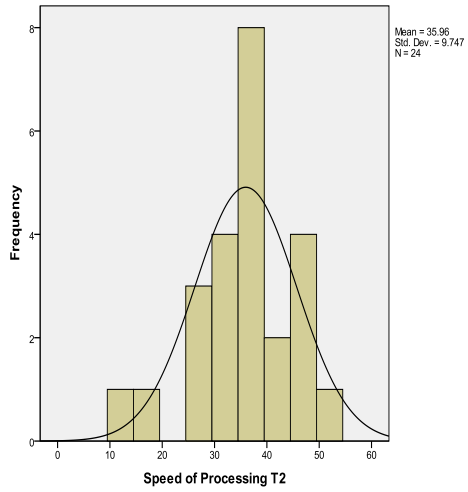
Variable	Skewness	Std. Error	Z	Kurtosis	Std. Error	Z
MCCB						
Speed of processing	.341	.550	0.620	-.124	1.063	-0.117
Attention/vigilance	-.445	.564	-0.789	-.899	1.091	-0.824
Working memory	-.672	.550	-1.222	-.173	1.063	-0.163
Visual learning	.530	.564	0.940	-.817	1.091	-0.749
Verbal learning	.084	.550	0.153	-1.067	1.063	-1.004
Reasonong/problem solving	.413	.550	0.751	-.661	1.063	-0.622
Social cognition	.331	.580	0.571	-.200	1.121	-0.178
UPSA						
Total score						
Social Functioning Scale						
SFS W	.944	.536	1.761	.489	1.038	0.471
SFS IP	-.777	.536	-1.450	-.093	1.038	-0.090
SFS IC	.334	.536	0.623	-1.111	1.038	-1.070

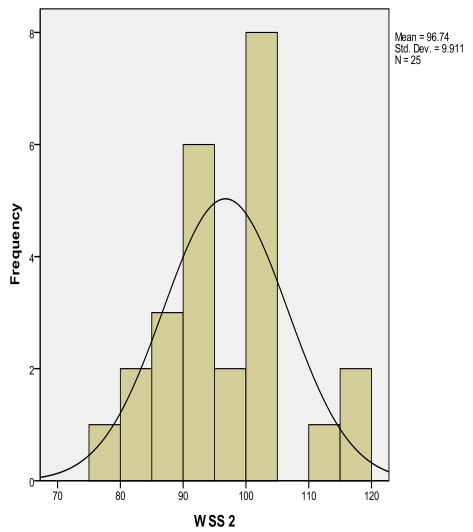
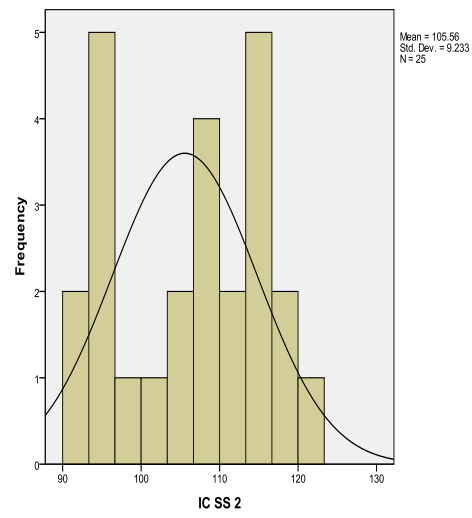
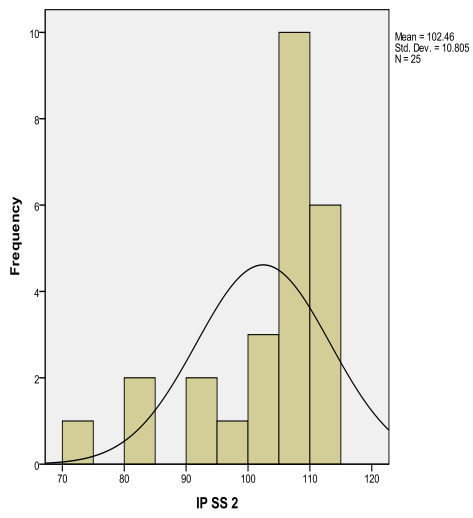
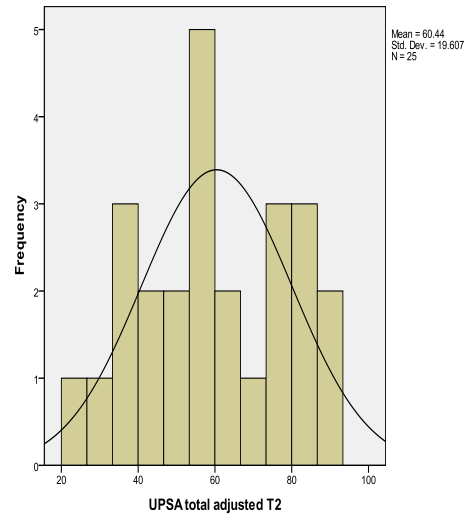
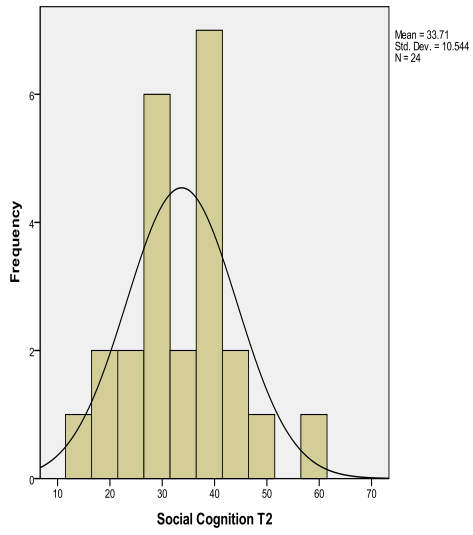
Histograms of all variables at Time 1



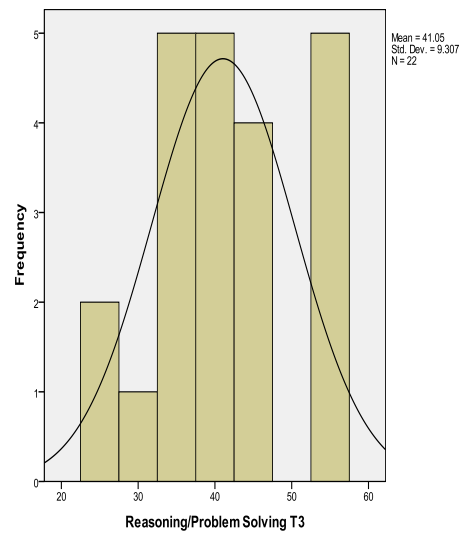
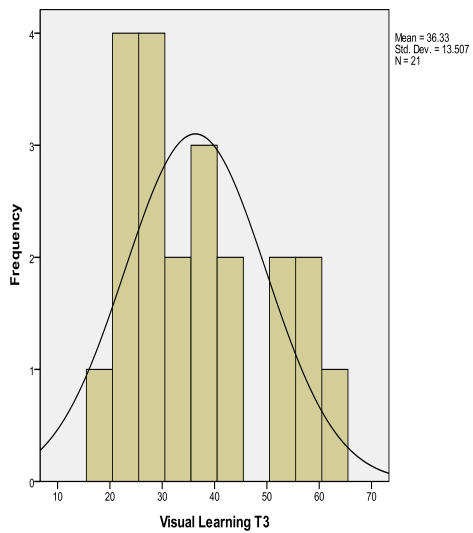
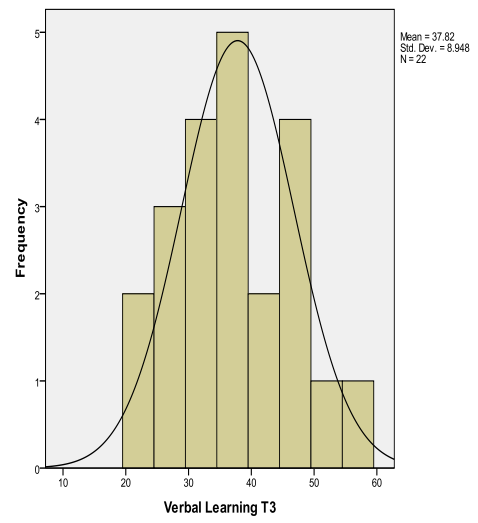
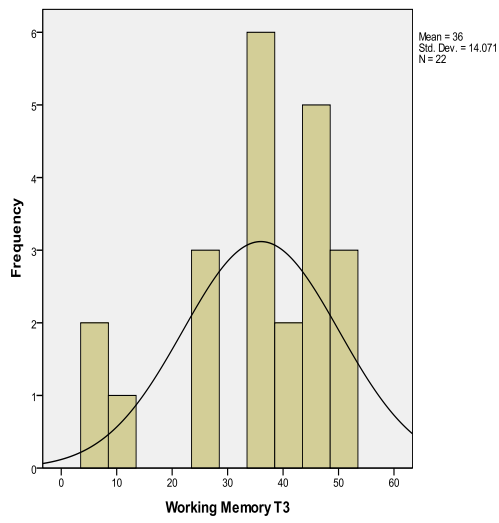
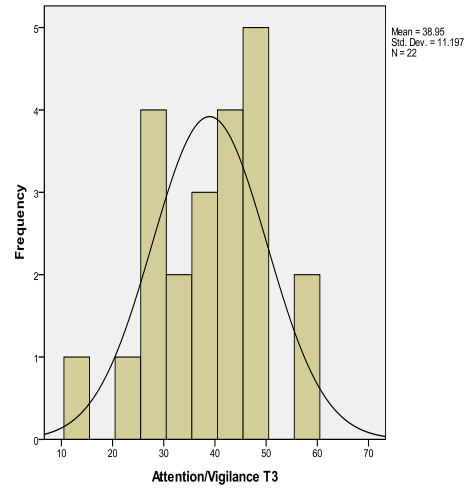
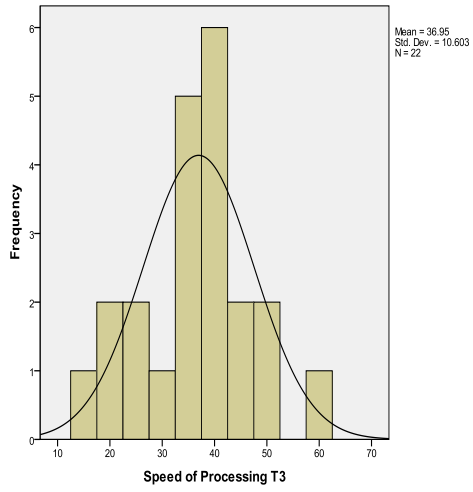


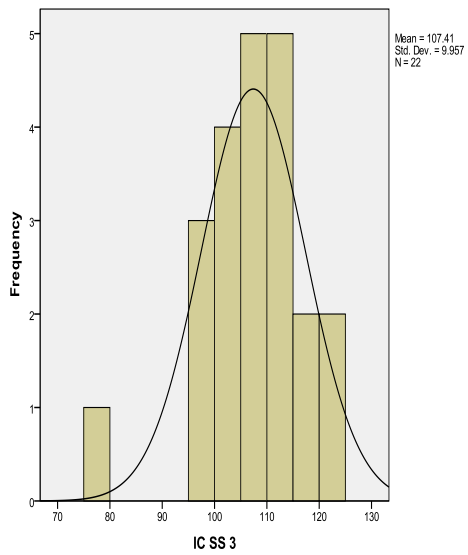
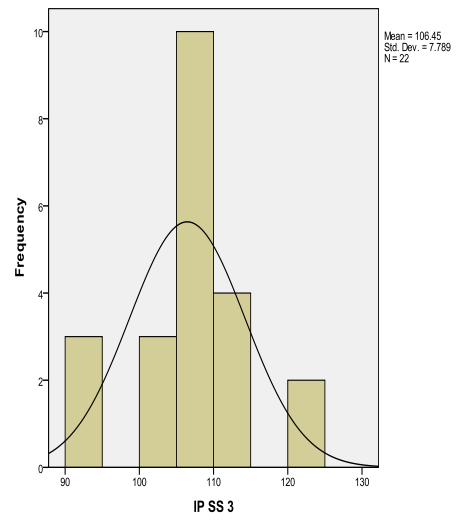
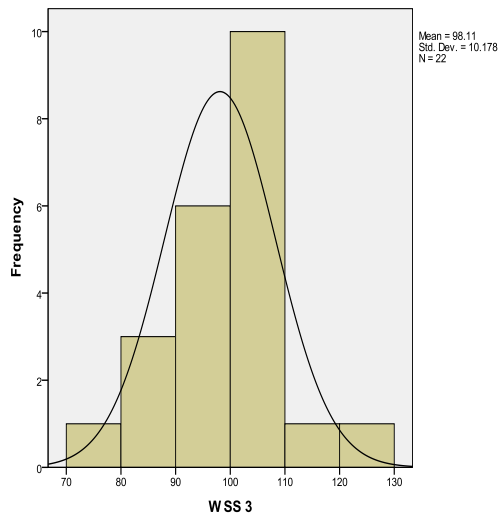
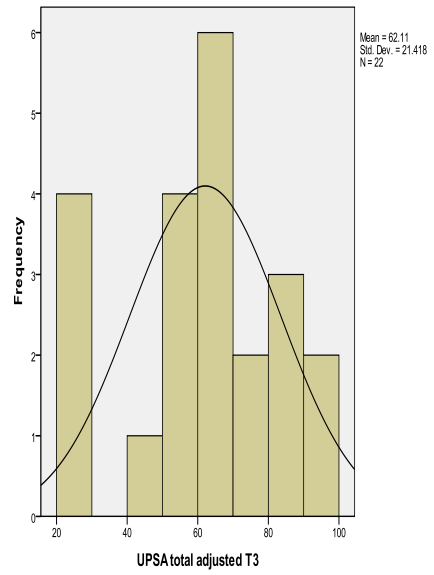
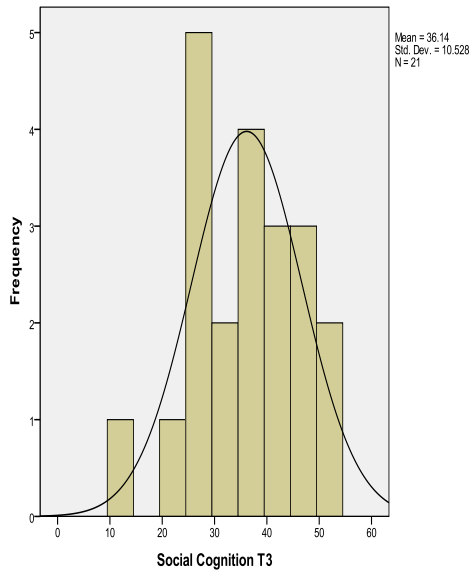
Histograms of all variables at Time 2



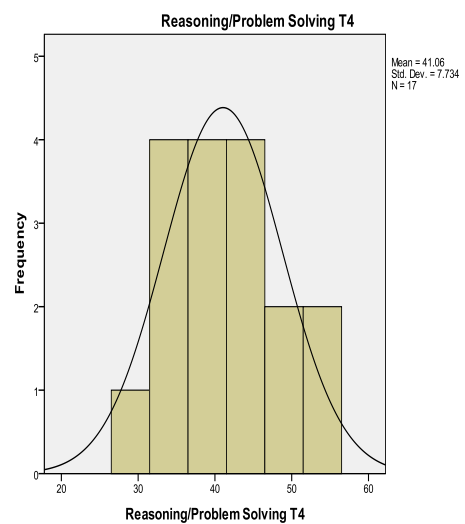
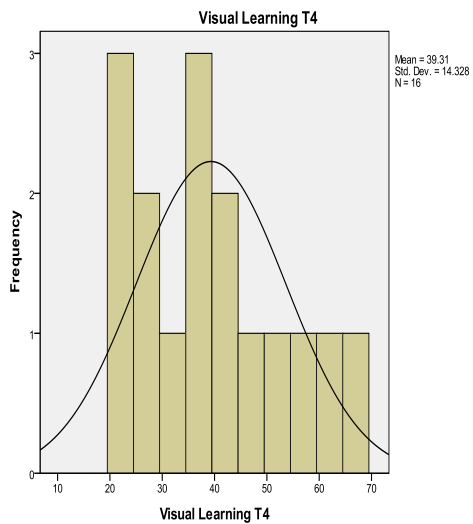
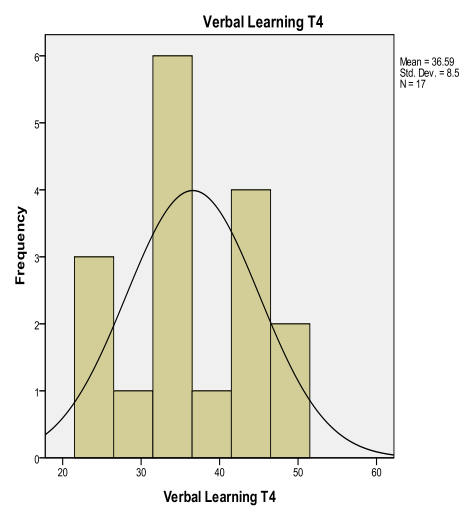
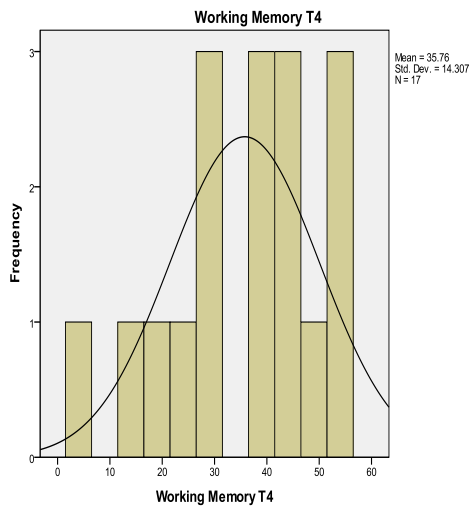
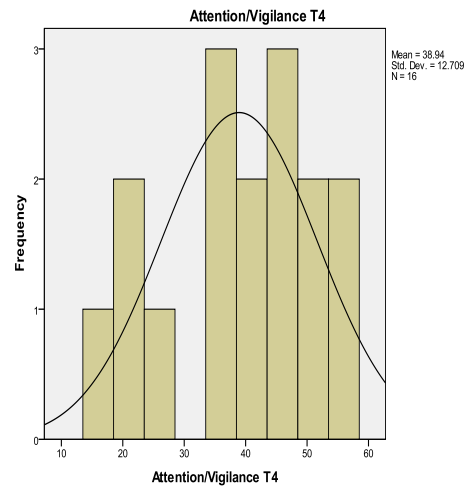
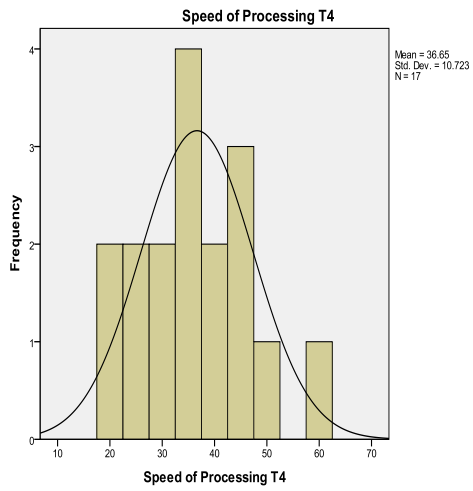


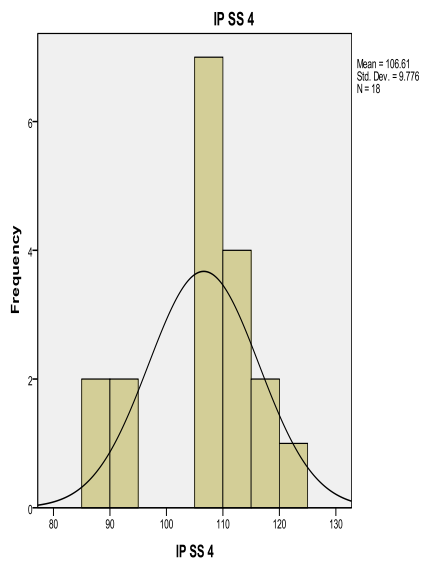
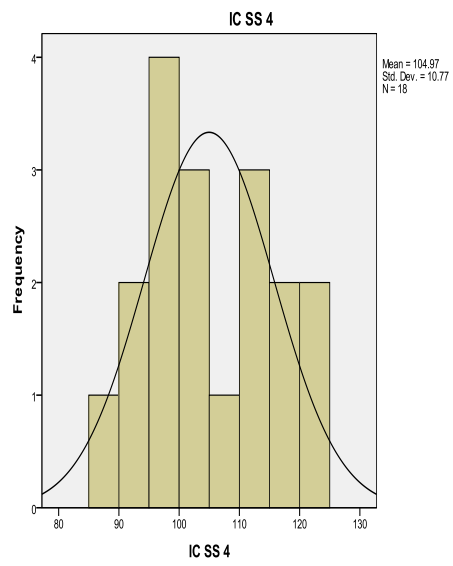
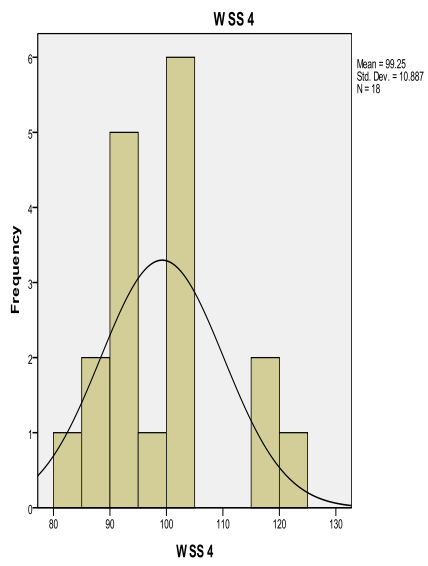
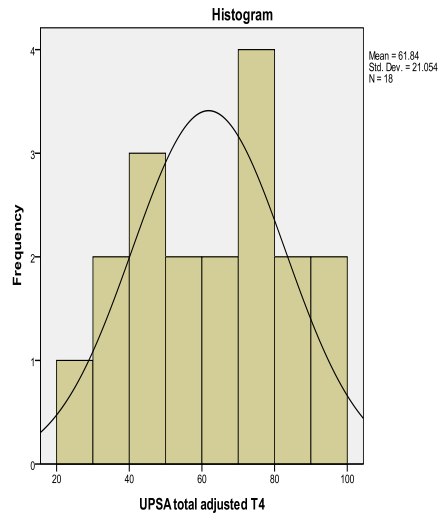
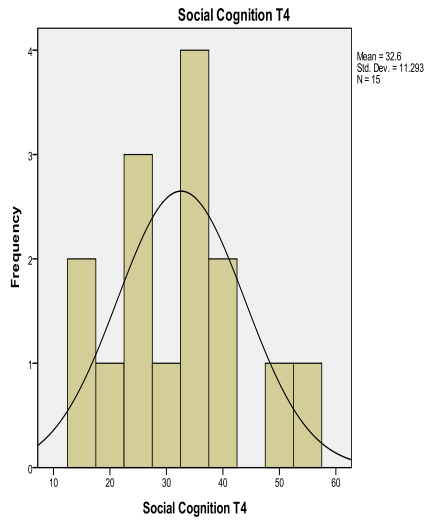
Histograms of variables at Time 3





Histograms of variables at Time 4





Appendix 11: Post hoc pairwise comparison tables

Table 1: speed of processing

(I) time	(J) time	Mean Difference (I-J)	Std. Error	Sig. ^a	95% Confidence Interval for Difference ^a	
					Lower Bound	Upper Bound
1	2	-3.941	1.405	.076	-8.168	.286
	3	-5.647*	1.328	.004	-9.643	-1.651
	4	-6.412*	1.430	.002	-10.713	-2.110
2	1	3.941	1.405	.076	-.286	8.168
	3	-1.706	1.487	1.000	-6.180	2.768
	4	-2.471	1.453	.650	-6.842	1.900
3	1	5.647*	1.328	.004	1.651	9.643
	2	1.706	1.487	1.000	-2.768	6.180
	4	-.765	1.059	1.000	-3.951	2.421
4	1	6.412*	1.430	.002	2.110	10.713
	2	2.471	1.453	.650	-1.900	6.842
	3	.765	1.059	1.000	-2.421	3.951

Based on estimated marginal means

a. Adjustment for multiple comparisons: Bonferroni.

*. The mean difference is significant at the .05 level.

Table 2: visual learning

(I) time	(J) time	Mean Difference (I-J)	Std. Error	Sig. ^a	95% Confidence Interval for Difference ^a	
					Lower Bound	Upper Bound
1	2	.500	1.586	1.000	-4.317	5.317
	3	-.375	2.097	1.000	-6.743	5.993
	4	-5.188	1.887	.089	-10.916	.541
2	1	-.500	1.586	1.000	-5.317	4.317
	3	-.875	2.536	1.000	-8.576	6.826
	4	-5.688	2.091	.095	-12.037	.662
3	1	.375	2.097	1.000	-5.993	6.743
	2	.875	2.536	1.000	-6.826	8.576
	4	-4.813	2.619	.516	-12.765	3.140
4	1	5.188	1.887	.089	-.541	10.916
	2	5.688	2.091	.095	-.662	12.037
	3	4.813	2.619	.516	-3.140	12.765

Table 3: reasoning/problem solving

(I) time	(J) time	Mean Difference (I-J)	Std. Error	Sig. ^a	95% Confidence Interval for Difference ^a	
					Lower Bound	Upper Bound
1	2	-3.824	1.332	.067	-7.830	.183
	3	-6.118*	1.150	.000	-9.577	-2.658
	4	-6.059*	1.282	.001	-9.915	-2.203
2	1	3.824	1.332	.067	-.183	7.830
	3	-2.294	1.495	.866	-6.790	2.202
	4	-2.235	1.335	.682	-6.253	1.782
3	1	6.118*	1.150	.000	2.658	9.577
	2	2.294	1.495	.866	-2.202	6.790
	4	.059	1.290	1.000	-3.823	3.941
4	1	6.059*	1.282	.001	2.203	9.915
	2	2.235	1.335	.682	-1.782	6.253
	3	-.059	1.290	1.000	-3.941	3.823

Based on estimated marginal means

a. Adjustment for multiple comparisons: Bonferroni.

*. The mean difference is significant at the .05 level.

Table 4: Composite score

(I) time	(J) time	Mean Difference (I-J)	Std. Error	Sig. ^a	95% Confidence Interval for Difference ^a	
					Lower Bound	Upper Bound
1	2	-2.000	1.267	.857	-6.066	2.066
	3	-4.500*	1.184	.018	-8.298	-.702
	4	-6.333*	1.378	.005	-10.754	-1.912
2	1	2.000	1.267	.857	-2.066	6.066
	3	-2.500	1.717	1.000	-8.007	3.007
	4	-4.333*	1.333	.046	-8.611	-.056
3	1	4.500*	1.184	.018	.702	8.298
	2	2.500	1.717	1.000	-3.007	8.007
	4	-1.833	1.308	1.000	-6.028	2.361
4	1	6.333*	1.378	.005	1.912	10.754
	2	4.333*	1.333	.046	.056	8.611
	3	1.833	1.308	1.000	-2.361	6.028

Based on estimated marginal means

a. Adjustment for multiple comparisons: Bonferroni.

*. The mean difference is significant at the .05 level.