The Effectiveness of Computerized Cognitive Rehabilitation Training Program in Improving Cognitive Abilities of Schizophrenia Clients

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Objective: The aim of this study was to evaluate the efficacy of a computer – based training program of attention, memory and executive functions in enhancing neuropsychological performances as well as functional outcome in clients with schizophrenia .

Method: A total of 15 clinically stable out patients with Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) criteria for schizophrenia, diagnosed with different types of schizophrenia: paranoid, disorganized, residual, based on DSM- IV-TR were selected to participate in this study. All patients were randomly selected using a conventional sampling method and assigned to 60 hours individual sessions of computer – assisted cognitive remediation (CACR).This was a pre-experimental study with pretest and posttest in a single group. Cognitive functions were checked with Continuous Performance Test (CPT), Wechsler Adult Intelligence Scale (Wds) and Prospective and Retrospective Memory Questionnaire (PRMQ). The symptoms of patients were measured with the Positive and Negative Syndrome Scale (PANSS). Remediation was performed utilizing the Rehacome® software. Patients received the cognitive remediation program including attention, concentration and working memory. All participants were followed up after an interval of one month and three months. Data were analyzed using repeated measures analysis.

Result: After 3 months, the findings showed that patients' scores improved in the time factor. Also, a significant improvement favoring cognitive remediation was found in several cognitive measures including Reaction Time (F = 4015p<.05, Eta = 0.242), Wds (F = 11.806, p<.05,Eta = .48) PRMQ1(F = 3.314, p<.05, Eta = 0.20) PRMQ7(F = 2.85, p<.05, Eta = 0.18).

Conclusion: Computer-assisted cognitive remediation training program was effective in improving the performance of schizophrenic patients. CACR did not have any effects on the positive and negative symptoms. Long- term follow-up studies are needed to confirm the maintenance of such improvements.

Schizophrenia is a devastating neurobiological disorder that typically strikes the brain function of adolescents and young adults, occurring in about 1 of every 100 people worldwide (1,2). The pathophysiology of schizophrenia remains puzzling (3, 4). During the last 30 years, substantial progress has been made in our understanding of the neurobiology and treatment of schizophrenia, and such advances have been accompanied by a modest overall improvement in outcome (5, 2). Cognitive impairment is a common, chronic disabling feature of schizophrenia (6). Deficits in cognitive functioning, including those in psychomotor speed, attention, memory and executive functions are thought to underline the severe functional disability associated with this illness (7, 8, 9, 10, 11). Moreover, the host of research has demonstrated functional outcome. Many approaches have been developed in the last fifteen years such as computer-assisted cognitive remediation (CACR). Patients with schizophrenia demonstrate some decline on the measure of neurocognitive functioning in attention, verbal and working memory and executive functions (12, 13, 14, 15). Several studies have shown a significant cognitive enhancement over various competencies (16, 17,18,19,20,35,36 and 37) whereas some studies showed heterogeneous conclusions about improvements resulting from

CACR (21, 22). In recent decades, several cognitive remediation techniques (computerized and non-computerized) have been designed for both individual and group settings. CACR interventions seem extremely relevant in schizophrenia, where neurocognitive alterations pervade all ability domains and strongly influence the patients' quality of life. Wykes and Vander Gaag (23) explain "the cognitive remediation" as a set of methods for teaching "the thinking skill" that focuses on cognitive deficits and holds as a common characteristic the reliance on material having no personal relevance to the individual. MC Guurk. and et al. (24) have reported the efficacy of cognitive remediation in schizophrenia and improvement in psychological functioning. Furthermore, CACR is well accepted amongst patients, and in recent years many researches have been done based on CACR to improve functional outcome in schizophrenic patients.

The Rehacom system (Hasomed GmbH, Germany) increases the capacity and efficiency of cognitive function and may be useful in improving cognitive disorders in patients with schizophrenia (35, 36, 37). This program has shown positive results in cognitive functions, in the ability to solve interpersonal problems and in autonomy and symptoms (25). Several studies showed a significant cognitive enhancement over various competencies. Benedict et al. (26) reported the effectiveness of cognitive – behavioral intervention in 15 clients with cognitive impairment associated with behavioral changes. In a randomized study, patients were randomly assigned to receive neuropsychological counseling or psychotherapy. After 2 weeks, the subjects of the active treatment group showed significant improvements in socially aggressive behavior compared to patients assigned to standard psychological counseling. Amato et al. (27) randomized 39 patients with schizophrenia to either 112 hours individual sessions of computer – assisted cognitive remediation or a control condition. The results showed that cognitive performances concerning attention / vigilance, verbal working memory and verbal learning memory and reasoning / problem solving improved significantly in the remediation condition while no differences were reported in the control condition between the 2 groups. However, no significant benefits of cognitive remediation were observed in non – verbal working memory and learning, speed of processing or functional outcome measures. Moreover, a number of studies have demonstrated that CACR may also affect psychotic symptoms and solve interpersonal problems in autonomy and symptoms. Taking into account all these factors, we assumed that offering computer – assisted cognitive remediation program to patients with schizophrenia could improve cognitive functioning. The present study investigated the effectiveness of computerized cognitive rehabilitation in improving cognitive abilities of schizophrenic patients.

Material and Methods
Clinical Trial Design
This was a pre-experimental study with pretest and posttest in a single group. The participants were assigned to receive CACR. Cognitive assessments were done four times for the patients at the beginning and at the end of the study. All participants were followed up after an interval of one month and three months. The assessment was conducted by a psychologist who was blind to the treatment assignment.
Participants
The participants were recruited by a conventional sampling method and were enrolled in the study from November 2011 to April 2012. A total of 15 clinically stable out patients with (DSM-IV-TR) criteria for schizophrenia signed the consent form and completed the baseline evaluation. The inclusion criterion for the study participants was the age of 18 or older. Diagnosis was made by expert clinicians through chart review and clinical interview using a symptom checklist allowing (DSM-IV-TR) criteria to be applied. Exclusion criteria were substance abuse or dependency during the previous 6 months, and having one or more clinical psychiatric disorders. Those participants who had acute medical diseases were removed from the study.
Assessment Symptoms
Psychiatric symptoms were assessed with the Positive and Negative Syndrome Scale (PANSS) (28). The symptoms were assessed following a semi-structured interview, referring to the month before the evaluation by the raters who used the scale routinely. Inter-rater reliability was measured and found to be high (intraclass correlation coefficient >0.9 for PANSS total scores). Inter –rater reliability of PANSS total scores and item scores were fairly good, with kappa scores between 0.60 and 0.70. PANSS items were divided into five factors according to (29): positive, negative, depressive, cognitive and excitement / hostility.
Neuropsychological Assessment
We used the Continuous Performance Test Identical Pair Version (CPTIP) to measure attention and vigilance. This requires the subject to respond whenever two identical stimuli appear in a row within a sequence of 150 rapidly flashed trials. We used the two– digit version and the 4 – digit version.
We retained (14) the index of perceptual sensitivity to signal the noise differences [d index] and (2) the response criterion; i.e., the amount of perceptual evidence that the subject required to decide whether a stimulus is a target [natural log of beta]. A valid CPTIP test was defined as a "d'index" greater than 0. We also considered the CPT numbers condition as an index of verbal attention as the stimuli can be verbally encoded to aid performance.

Cognitive Function

Working memory was measured with the digit span forward and backward from the Persian version of the Revised Wechsler Adult Intelligence Scale (WAIS) Test (30). The participants were given a number string and were asked to repeat it backwards (Digit span Back war) (e.g., 936) (from 2 digits to a maximum of 8 digits). The measure was number correct for each condition. In one Iranian study, the reliability and validity of WAIS-R were studied (31). The WAIS-R subscales showed a reliability of 0.69 to 0.87 on test- retest stability, and their internal consistency was 0.77 to 0.88 with a split-half coefficient WAIS administered by a PhD student of psychology (32).

All participants completed the Prospective and Retrospective Memory Questionnaire (PRMQ).The PRMQ is a 16 item, self – report inventory that measures the frequency with which perceived memory difficulties occur in everyday life on a 5 point Likert- type scale ranging from 0 (never) to 5 (very often)

The PRMQ which measures prospective memory lapses, for example: "How often do you forget something that you were told a few minutes before"? Eight items of this questionnaire measure retrospective memory lapses (e.g., How often do you forget appointments if you are not prompted by someone else or by a reminder such as a diary or a calendar. Prior research supports the internal consistency (Cranach's alphas≥. 80), factor structure (33) and predictive validity (34) of the prime.

Intervention: Computer-Assisted Cognitive Remediation Therapy

(REHACOM® modules)

This therapy consisted of 20 individual sessions, each of which lasted for 60 minutes with participants completing two sessions per week for about 18 weeks. A psychologist conducted CACR on a computer using the Rehacome® software. This program enables patient progression and feedback. Four cognitive functions were trained using diverse exercises: attention / concentration, working memory and executive functions. For more details about the Rehacome modules, visit the Rehacome website at http: "www.hasomeb.de. One month and three months after the completion of the training, a follow up assessment was carried out. No contacts were made between the members of the research team and the participants during this period. The tasks applied at pretest, posttest and follow up were all the same as those used during the training.

Attention and Concentration (REHA-AUFM)

In the procedure, attention and concentration (REHA-AUFM), a separately presented picture is compared to a matrix of picture. The patient should recognize a picture (symbols, items, animals or abstract figures) shown separately and select it from a matrix. The abilities to differentiate and concentrate are taught simultaneously.

Memory (REHA-MEMO)

In the training procedure, "topological (or visual-spatial) memory (REHA-MEMO)", every training task is divided into two stages: the acquisition stage and the reproduction stage. In the acquisition stage, the patient's task is to memorize the content and the placement of the pictures. During the reproduction stage, the pictures are covered with one picture displayed separately (with no cover). The patient's task is to locate the picture's pair from the matrix of the covered pictures.

Attention and Vigilance

This program aims to improve vigilance or sustained attention, and it trains the ability to sustain attention over a relatively long period while items are presented under time- critical conditions. The client's task is to monitor a conveyor belt and pick out the items that differ in one or more details from the sample objects. Objects moving past on objects moving past the conveyor belt must be continuously compared with one or more sample objects.

Memory-Physiognomic Memory

This program uses realistic material to train clients to recognize faces and assign names and occupations to faces. Faces are displayed from different perspectives. The client decides whether he/she saw this person before. At higher levels of difficulty, the client is also required to memorize additional information (the person's name and occupation). The client must memorize the faces that are present in the learning phase, and then he/she is asked to recognize them in a sequence of pictures. At higher levels of difficulty, a name and an occupation are assigned to each face, and the client must then find the face that goes with a particular name or occupation.

Statistical Analysis

First, we compared the group members on the demographic, clinical and cognitive measures at baseline using t – tests (continuous variables) and chi – square analyses (categorical variables.(

Second, we used an analysis of repeated measures. Measures of pretest, posttest, follow-up1 and follow-up 2 were used as the time factor and PANSS (positive – negative signs as a group) as the between factor. In addition, we examined the effect of interaction Time* group.

Results

The mean and standard deviation of all the variables were reported in Table 1. The findings show that reaction time was reduced from the pre to the follow up 2. In contrast, Wds' scores were increased from the pre to the follow up 2. The PRMQ1 was reduced from the pre to the post test, while the PRMQ1 was increased in the follow ups (1 and 2). There is a similar pattern for the PRMQ7.

**Table 1: The Mean and Standard Deviations of the Study Variables in Terms of the Time Factor and Group**

Pre		Post		Follow1		Follow2	
Positive	**Negative**	**Positive**	**Negative**	**Positive**	**Negative**	**Positive**	**Negative**
2.00	1.33	1.67	0.667	1.67	2.00	1.44	1.17
1.33	0.50	0.33	2.50	1.11	1.33	1.56	1.50
146.67	148.17	148.00	147.00	147.22	146.67	147.00	147.33
505.00	500.50	503.67	483.83	465.67	475.67	443.33	456.67
5.56	5.17	7.56	6.33	8.11	7.67	6.89	5.50
2.33	3.17	1.89	1.67	1.78	3.00	2.56	2.67
2.11	2.50	2.33	2.00	1.67	1.83	2.67	1.50
2.44	2.00	1.78	2.50	2.67	2.67	2.67	2.17
2.33	2.33	2.57	2.17	2.33	2.67	1.89	2.67
2.00	1.67	1.56	2.17	1.67	2.67	2.67	2.00
2.11	2.67	2.00	1.17	1.89	2.00	2.89	1.67
1.89	1.83	1.56	1.67	2.00	2.17	2.67	2.50
2.56	2.33	1.67	2.17	1.89	2.17	2.44	2.17
2.78	2.33	1.67	2.67	1.67	2.50	2.67	1.83
2.89	2.33	2.11	2.00	2.00	2.67	2.44	2.50
2.22	2.00	1.22	1.83	1.67	2.33	2.11	2.17
2.11	2.50	1.89	2.00	1.78	2.50	2.22	2.33
2.67	1.83	2.22	1.67	1.78	2.00	2.11	2.00
1.89	2.00	1.67	2.33	1.78	2.67	2.44	2.00
2.11	2.33	1.89	1.83	1.89	2.33	2.89	2.50
2.67	2.17	1.56	2.67	1.78	2.33	2.67	2.33
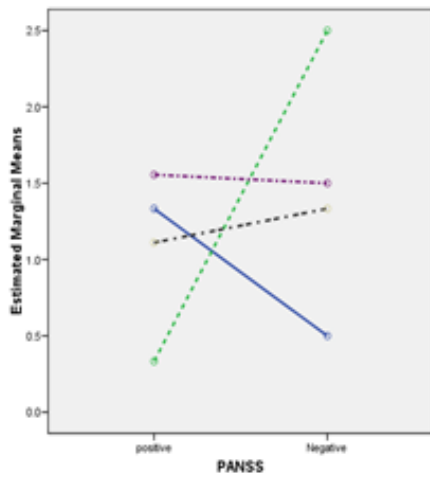
(a)OMISSION
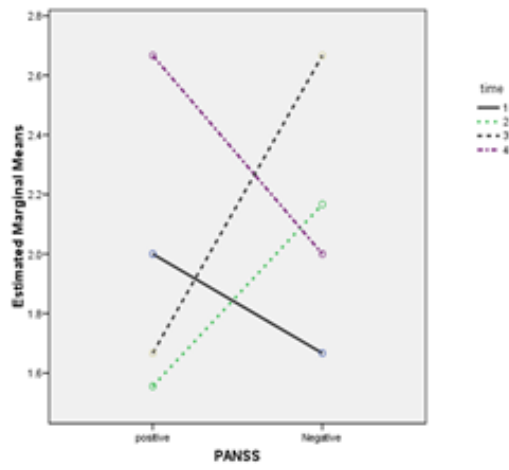
(b)PRMQ5
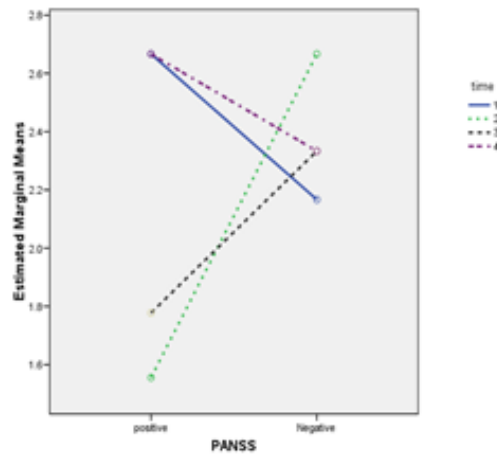
(c) PRMQ16

Figure 1: Interaction Effect between Time and Group

First, we tested the assumptions of repeated measures as the analyzed model. Mauchly's test of sphericity was not significant for any of the measures. In addition, Levene's test of equality of error variances was not significant in any of the dependent variables. We did not have any missing data. Thus, there were enough reasons to use multivariate repeated measures.

The findings showed that the patients' scores improved in the time factor. There were significant differences in the reaction time, PRMQ and Wds. Significant improvement favoring cognitive remediation was found for several cognitive measures including reaction time (F = 4.15 p < .05, Eta = 0 .242), Wds (F = 11.806, P < .05, Eta = .48), PRMQ1(F = 3.314, p < .05, Eta = 0.20), PRMQ7 (F = 2.85, P < .05, Eta = 0.18). No significant differences were observed in terms of the factor group. The post hoc tests showed that the reaction time in the post test was significantly different from the reaction time of the follow up 2 (D2-4 = 43.75, p < .05). The Wds' scores at baseline was differentiated with the follow up 1 (D1-3 = -2.53, p < .001). Also, the Wds' scores was different between the follow- up 1and follow-up 2 (D3-4 = 1.69, p < .001). Although the results of the univariate tests revealed a significant difference between the PRMQ1'scores and the PRMQ7' scores, the results of the post hoc test did not show any significant differences.

There was an interaction effect between time × group. The interaction effect was found for the omission in the CPT test (F = 4.33, P < .05, Eta = 0.25), PRMQ5 (F = 3.489 P < .05, Eta = 0.212) and PRMQ16 (F = 3.64 P < .05, Eta = 0.219). The post hoc tests showed that in patients with positive signs, the omission in the follow-up 2 differed significantly with the omission of the posttest (D4-2 = 1.22, p < .05) (Figure 1a). There was a similar pattern for PRMQ5. In patients with positive signs, the results of the follow-up 2 differed significantly from those of the posttest (D4-2 = 1.11, p < .05) (Figure 1b). In addition, the post hoc tests showed that in patients with positive signs, the PRMQ16 in the post test was significantly different compared to baseline (D2-1 = -1.11, p < .05); and in the same group, the PRMQ16 in the follow-up 2 was significantly different from the posttest (D2-4 = -1.11, p < .05)(Figure 1c).

Discussion

We aimed to find whether computer – assisted cognitive remediation (CACR) is able to modify cognitive performance in remitted patients with schizophrenia. Using a program consisting of 20 training sessions of 4 cognitive functions (attention / concentration, working memory, executive function) by means of the Rehacom® software, we found that CACR could improve performance in attention / vigilance, working memory and prospective and retrospective memory.

Overall, the cognitive performance and functional capacity of the participants were improved. All patients were compared after the follow – up. Based on the results of this study, attention / vigilance, working memory and prospective and retrospective memory were improved in all patients after they received CACR. We also found that the reaction time was increased from the posttest to the follow up 2. That is, the treatment did not have any effects in the long term. The working memory scores were reduced from the baseline to the follow up 1, but it was increased from the follow 1to the follow 2, meaning that the treatment had a positive effect in the long term. In patients with positive signs, the number of omissions was increased from the posttest to the follow up 2, meaning that the treatment did not have any effects in the long term. In patients with positive signs, the PRMQ5 was increased from the posttest to the follow up 2, meaning that the treatment did not have any effects in the long term. In patients with positive signs, the PRMQ16 was reduced from the baseline to the posttest, which means that the treatment had a positive effect in the long term. In patients with positive signs, the PRMQ16 was increased from the posttest to the follow up 2, meaning that the treatment did not have any effects in the long term. We observed no effect of CACR in the positive or negative symptoms. However, the follow up period was certainly too short to observe such effects which may take a relatively long time before becoming apparent.

In an exploratory analysis, we observed that a significant time × group interaction was only observed for reaction time in CPT task (omission) and prospective and retrospective memory (p = 16). An important finding of this study was the absence of a significant effect of CACR on positive and negative symptoms. Previous studies such as one conducted by Amato et al., (22) observed no improvement in positive or negative symptoms measured by Positive and Negative Syndrome Scale (PANSS).

In summary, the present study indicated an improvement in cognitive functioning. However, no differential effect was observed in different levels of differential improvement in patient relevant outcome measures. Thus, CACR was effective in improving the performances of schizophrenic patients in attention, working memory and prospective and retrospective memory. These findings corroborate with those of previous studies (35, 36, 37). There were several limitations in this study. First, the participants were not randomly assigned to CACR. Second, we did not find a clear effect of CACR on changing the symptoms as measured by the PANSS. Third, we only reported the results of one group comprising of 15 participants. The sample size of the previous studies was about 20 but due to difficulty reaching them, we selected 15 participants. In this study, unfortunately, patients received antipsychotic medication, and we could not compare the efficacy of antipsychotic medication on the patients' functioning. Future studies are necessary to determine the effective framework for antipsychotic medication on patients' functioning. Our encouraging

finding will need to be replicated with a larger sample size. Even with these limitations, the results of this study indicate that CACR may be effective in clinical, neuropsychological and functional outcomes. More studies with longer follow-up periods are needed to generalize the results of this study and to verify the effects of this cognitive training program.

Conclusions

Computer-assisted cognitive remediation training program was effective in improving the performance of schizophrenic patients. CACR did not have any effects on the positive and negative symptoms. Long- term follow-up studies are needed to confirm the maintenance of such improvements.

Acknowledgments

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