Title: A Short Course Computer-Based Cognitive Remediation in Patients With Schizophrenia Spectrum Disorders: A Randomized Clinical Trial

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Abstract:

Introduction: Cognitive remediation is used to improve cognitive functioning in patients with schizophrenia. Most of the previous studies had incorporated a long duration of a rehabilitation program. This study aims to evaluate the effect of a short course and easy to implement computer-based cognitive remediation on the cognitive performance in patients with schizophrenia spectrum disorders using a randomized controlled trial design.

Method: Sixty-two patients with schizophrenia spectrum disorders were enrolled in Roozbeh Hospital (Tehran, Iran) and were randomized to either receive a cognitive remediation program added to the standard pharmacological treatment (n=31) or the standard treatment alone (n=31). The remediation consisted of ten sessions of the cognitive training provided 2-3 times a week by applying the Cogpack software. The cognitive performance was assessed in attention, memory and executive function before and after the interventions by using the respective tests of the Cambridge Neuropsychological Test Automated Battery (CANTAB).

Results: This study did not demonstrate any significant improvement in attention and executive function in the experimental vs control group. Nonetheless, we observed modest improvements in some aspects of visual memory (first trial memory score, F=9.152, P< 0.001, Cohen’s d=0.40; Mean errors to success, F= 6.991, P= 0.011, Cohen’s d=0.14; stages completed on first trial, F= 7.155, P= 0. 010, Cohen’s d=0.71; Total errors, F= 5.730, P= 0.020, Cohen’s d=0.53).

Conclusion: We observed only modest improvements in the patients' cognitive functioning after a short-course of cognitive remediation. The short duration of the training and lack of a comprehensive rehabilitation plan may explain the findings.

Keywords: Cognitive Remediation, Schizophrenia, Cognitive rehabilitation, Short Course
Introduction

Schizophrenia is a chronic mental illness with various presentations. Kraepelin and Bleuler proposed some deficits in cognitive domains in schizophrenia; including attention, memory, reasoning, problem-solving, and other cognitive skills (Chattopadhyay, Nayak, Patil, & Chate, 2012). Although for several decades, cognitive impairment in schizophrenia was neglected, recently, they have been considered as the core feature of illness and strongly correlated with social deficits and poor outcomes (Harvey, 2013), (Revheim et al., 2006), (Kurtz, Seltzer, Shagan, Thime, & Wexler, 2007), (Keefe et al., 2010).

Furthermore, the experts agreed that six cognitive domains including perception, working memory, attention, executive functions, long-term memory, and social cognition are affected in schizophrenia (Carter & Barch, 2007). Despite the growth of knowledge, there is no established medication to improve cognitive performance in schizophrenia (Barch et al., 2008). It seems current pharmacological treatments do not improve the cognitive deficits (Keefe & Harvey, 2012), (Choi, Wykes, & Kurtz, 2013).

A novel and safe psychosocial treatment is providing cognitive remediation therapy (CRT) by using computer software. This intervention can be provided in paper-pencil or computer-based formats.

In recent years, several pieces of literature have consistently demonstrated the benefits of long-term CRT on cognition and psychosocial functioning with moderate effect size (Katsumi, Hoshino, Fujimoto, & Niwa, 2015), (McGurk, Twamley, Sitzer, McHugo, & Mueser, 2007), (Grynszpan et al., 2011), (Deste G, 2019; Kurtz & Richardson, 2011). In 2016 a before-after study was conducted in Iran by Sharifi et al (Sharifi, Sedighnia, Ataie, Tabatabae, & Tehranidoost, 2016). This study has demonstrated the efficacy of CRT in schizophrenia. In Iran, as a developing country, providing psychosocial interventions may be influenced by some different obstacles. CRT as a psychosocial intervention, is faced with more barriers. Feasibility of interventions, patients’ socio-economic state, cost of services, and poor treatment adherence are among these barriers.
This study aims to evaluate the effect of a short course and easy to implement computer-based CRT on the cognitive performance in patients with schizophrenia spectrum disorders using a randomized control trial in a developing country setting.

Material and Method:

2.1. Design

This study was conducted at Roozbeh Hospital in Tehran, Iran in 2017-2018 and was registered in the Iranian Registry of Clinical Trials (IRCT2016011810782N2). We considered all aspects of the Declaration of Helsinki. We compared a computerized CRT program added to the standard treatment versus the standard treatment. In our setting, standard treatment consists of pharmacotherapy along with psychoeducation. The intervention was clearly explained to the participants. After obtaining a written informed consent the patients were assigned to the two groups by applying the block randomization design. After an initial assessment, sixty-two patients were randomized to either the intervention (standard treatment and CRT program, n=31) or the control group (standard treatment alone, n=31).

A trained psychologist and a psychiatry resident assessed the clinical and cognitive performance of all participants. Demographic characteristics were documented in forms. After receiving ten rehabilitation sessions in the intervention group and after 30+/−2 days from baseline assessment in the control group, the reassessment was performed. We should note that transportation was free for all of our participants.

2.2. Participants

The participants were enrolled in Roozbeh Hospital, a referral psychiatric hospital in a metropolitan city, Tehran. Based on the eligible criteria, patients should meet the DSM IV-TR criteria for schizophrenia or schizoaffective disorder based on the Persian copy of Structured Clinical Interview for DSM IV (SCID-I). (Sharifi et al., 2004) Participants were clinically stable, and there was no modification in their medications for at least three weeks before the study. Clinical stability was confirmed by the PANSS scores less than 50 and the CGI scores less than 4.
throughout the project. Inclusion criteria were: age 18-55, at least two years passed since the onset of illness, obtained informed consent, and at least 8th grade education. The exclusion criteria were the followings: intellectual disability (IQ<70), substance use comorbidity except for nicotine and caffeine, being treated by ECT within the past six weeks, any history of head trauma with loss of consciousness, neurological disease, receiving antihistamine medications, uncorrected visual impairment, and physical disabilities interrupt the computer-based exercises. Furthermore, patients were excluded in case of worsening of symptoms or need to change their medication or dosage.

2.3. Treatment

In the intervention group, CRT by using Cogpack software was provided (Marker, 1987). The Cogpack contains 64 tasks. We selected twenty-first tasks based on cultural and linguistic considerations. These 21 tasks were the followings: Ball, borders, comparison, confusion, eye witness, labyrinths, logic, math A, math B, multiply, memory, new or not, on the road, piece work, reaction, route, scan, search, sequence, UFO and visuomotor.

These tasks were designed based on difficulties in three levels: easy, intermediate, and difficult. In this study, regardless of the patient's performance, assignments were routinely started from the easy level, and after the first three sessions, the patients entered the intermediate and after the seven session, he/she takes the difficult level. We proposed a modified shortened version of the intervention because of limited resources in Iran. Ten sessions of CRT held 2-3 times a week. The duration of each session was about 60 to 75 minutes. During the intervention, the clinician explained the instructions for each task to the patients. The patients’ performances were recorded, and patients received feedbacks during the session and over the course of rehabilitation. This software allowed the therapist to have a profile of cognitive performance for each patient. Three cognitive functions were involved including attention/concentration, visual memory, and executive functions. CRT was provided by psychologists, social workers, or occupational therapists who had previously participated in a one-day workshop. All of the therapists received weekly supervision from an expert psychiatrist. All medical information was recorded. This information included the type and dosage of medications, duration of administration, and any changes made in treatment.

2.4.1. Clinical Assessment
A blind investigator assessed the participants, using the Positive and Negative Syndrome Scale (Kay, Fiszbein, & Opler, 1987), the Clinical Global Impression (CGI) (Guy, 1976), and the Wechsler Adult Intelligence Scale (Wechsler, 1981).

2.4.2. Neurocognitive Assessment

We used the CANTAB software (Cambridge Neuropsychological Test Automated Battery) for cognitive assessment (Robbins et al., 1994). This software can present deficits in various cognitive domains including working memory, decision-making, attention, executive function, and visual memory. Furthermore, CANTAB tests could provide an interpretation of patient performance. In this study, we used version 3.2 of CANTAB, and the software was administered by a trained psychologist.

The patients’ cognitive function was evaluated by using some tests of CANTAB battery. These tests were stop-signal task (SST) and choice reaction time (CRT) to assess attention, pattern recognition memory (PRM), and paired associates learning (PAL) to examine visual memory and stockings of Cambridge (SOC), stop-signal task (SST) and intra-extra dimensional set shift (IED) to evaluate executive function.

2.4.3. Psychosocial Assessment

Participants’ performance was assessed by GAF (Global Assessment of Functioning), (Hilsenroth et al., 2000), and the quality of life was assessed by the Persian version of WHO QOL-Brief (World Health Organization Quality of Life-Brief version) (Nejat S, 2006).

2.5 Statistical Analysis

Regardless of whether the intervention was completed or not, all analyses were performed for all patients using the SPSS software version 21. First, all variables (88 variables) assessed for normal distribution using the Kolmogorov-Smirnov test. 36 variables did not have a normal distribution. We normalized these variables used lg10, but 15 out of 42 pretests and 13 out of posttests did not have normal distribution still, we used Mann Whitney U Test for these variables. The baseline demographic and clinical characteristics were compared between the two groups by applying t-
tests or chi-square. After comparing two groups on demographic and baseline clinical characteristics, improvements in cognitive and social functioning and psychotic symptoms were compared between two groups using analysis of covariance (ANCOVA). We used the t-test for 3 variables that did not meet the assumptions required for ANCOVA. (P-value was set at 0.05). Cohen’s d was calculated for effect size estimation.

3. Results

3.1 Patient Flow and Baseline Characteristics

Patients’ recruitment had been done from August 2015 to March 2017 in Roozbeh Psychiatric Hospital. In this study, seventy-four clients met the eligibility criteria and signed informed consent. However, 12 patients were excluded before allocation. The reasons for this exclusion were the withdrawal of consent (4 patients), worsening of symptoms (5 patients), the presence of some medical problems (2 patients), and enrollment in a full-time job (one patient). Therefore, 62 clients were randomized and completed the pretest (31 patients in each group). Four out of thirty-one participants in the intervention group received less than ten rehabilitation sessions. Six out of 62 patients dropped out during the program (three in the intervention and three in the control group). Reasons for dropping out were worsening of symptoms (three patients), changing the place of residence (one patient), withdrawal of consent (one patient). At the end of the study, 56 out of 62 patients were re-evaluated by CANTAB, PANSS, GAF, CGI, and WHO-QoL-Bref (Figure 1).
Assessed for eligibility and obtained participants' consent (n=74)

Excluded (n=12)
- Refused to participate (n=4)
- Worsening of symptoms (n=5)
- Some medical problems (n=2)
- Full-time jobs (n=1)

Randomized (n=62)

Allocated to Cognitive Remediation intervention (n=31)
- Completed 10 cognitive rehabilitation sessions (n=27)
- Received less than 10 cognitive rehabilitation sessions (n=4)

Allocated to control (n=31)
- Received treatment as usual (n=31)

Analyzed (n=28)
- Excluded from the analysis (declined to participate) (n=3)

Fig 1. Flow diagram of the randomized clinical trial
3.2 Baseline demographic and clinical variables

There was no statistically significant difference in age, gender, educational level, marital status, employment, prescribing first or second-generation antipsychotics, and antipsychotics' equivalent dosage between two groups (intervention and control). Furthermore, there were no statically significant differences between the groups at baseline in clinical variables (Table 1).

Table 1. Baseline demographic and clinical data of patients in the CRT and control group.

<table>
<thead>
<tr>
<th></th>
<th>CRT group n=31</th>
<th>Control group n=31</th>
<th>Statistics t test p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>35.9 (8.5)</td>
<td>38.9 (9.5)</td>
<td>-1.32</td>
</tr>
<tr>
<td>WASI IQ scores</td>
<td>86 (11)</td>
<td>86 (11)</td>
<td>0.214</td>
</tr>
<tr>
<td>Illness duration(Month)</td>
<td>150.7 (87.5)</td>
<td>141.6 (100.5)</td>
<td>0.380</td>
</tr>
<tr>
<td>Duration of using antipsychotics(Month)</td>
<td>125.5 (93.2)</td>
<td>125 (98)</td>
<td>0.021</td>
</tr>
<tr>
<td>The equivalent dose of haloperidol for typical antipsychotics (mg)</td>
<td>4.5 (6.1)</td>
<td>3.5 (4.6)</td>
<td>0.736</td>
</tr>
<tr>
<td>The equivalent dose of risperidone for typical antipsychotics (mg)</td>
<td>2.53 (2.69)</td>
<td>3.38 (3.67)</td>
<td>0.301</td>
</tr>
</tbody>
</table>

3.3 Baseline cognitive variables

There were no statically significant differences between the two groups in attention, executive function, and visual memory at the baseline evaluation.

3.4 Cognitive outcomes

In this study, CRT and SST tests were used to assess the attention. At the end of the study, there was no statistically significant difference between the two groups in the CRT and SST. Attention scores (CRT and SST tests) in the two groups at baseline and retest are presented in Table 2.
Table 2. Attention variables (CRT and SST test) at baseline and retest in the two groups.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Retest</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CRT group</td>
<td>Control group</td>
<td>CRT group</td>
</tr>
<tr>
<td></td>
<td>n=31</td>
<td>n=31</td>
<td>n=28</td>
</tr>
<tr>
<td>Mean (S.D.)</td>
<td>Mean (S.D.)</td>
<td>Mean (S.D.)</td>
<td>Mean (S.D.)</td>
</tr>
<tr>
<td>* CRT Percent commission trials</td>
<td>0.1 (0.3)</td>
<td>0.2 (0.5)</td>
<td>0.1 (0.5)</td>
</tr>
<tr>
<td>* CRT Percent correct trials</td>
<td>99.1 (1.2)</td>
<td>98.2 (2.7)</td>
<td>99.5 (0.8)</td>
</tr>
<tr>
<td>* CRT Percent omission trials</td>
<td>0.07 (0.2)</td>
<td>0.2 (0.7)</td>
<td>0.07 (0.2)</td>
</tr>
<tr>
<td>CRT Mean correct latency</td>
<td>556.1 (186.7)</td>
<td>624.6 (170.9)</td>
<td>494.9 (160.6)</td>
</tr>
<tr>
<td>* CRT Total commission errors</td>
<td>0.1 (0.3)</td>
<td>0.17 (0.4)</td>
<td>0.0 (0.0)</td>
</tr>
<tr>
<td>* CRT Total correct trials</td>
<td>99.1 (1.2)</td>
<td>98.6 (2.4)</td>
<td>99.5 (0.8)</td>
</tr>
<tr>
<td>* SST Direction errors on stop and go trials</td>
<td>1.9 (2.2)</td>
<td>2.2 (3.8)</td>
<td>2 (3.1)</td>
</tr>
<tr>
<td>** SST Proportion of successful stops (last half)</td>
<td>0.6 (0.1)</td>
<td>0.57 (0.1)</td>
<td>0.62 (0.13)</td>
</tr>
<tr>
<td>SST Median correct RT on GO trials</td>
<td>866.8 (251.2)</td>
<td>873.8 (230.9)</td>
<td>841.4 (266.3)</td>
</tr>
<tr>
<td>SST SSD (5%) (last half)</td>
<td>562 (131.4)</td>
<td>579.6 (126.2)</td>
<td>581.2 (127.7)</td>
</tr>
<tr>
<td>**SST SSRT (last half)</td>
<td>283.2 (127.4)</td>
<td>296.2 (140.2)</td>
<td>260.1 (127.7)</td>
</tr>
</tbody>
</table>

* We used Mann Whitney U Test for this variables (did not have normal distribution)

** We used t test for this variables (did not meet assumptions required for ANCOVA)
RRM and PAL test were utilized to assess visual memory. There was no statically significant
difference between groups in the PRM test. It should be mentioned, Analysis of Covariance
(ANCOVA) revealed a significant difference in five out of seven score in PAL test (first trial
memory score, F=9.152, P= 0.004, Cohen’s d=0.40; Mean errors to success, F= 6.991, P= 0.011,
Cohen’s d=0.14; stages completed on first trial, F=7.155, P= 0.010, Cohen’s d=0.71; Total errors,
F=5.730, P=0.020, Cohen’s d=0.53) in posttest. These results are presented in Table 3.

**Table 3. Visual memory variables (PRM and PAL test) at baseline and retest in the two groups.**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Retest</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CRT group</td>
<td>control group</td>
<td>CRT group</td>
</tr>
<tr>
<td></td>
<td>n=31</td>
<td>n=31</td>
<td>n=28</td>
</tr>
<tr>
<td>Mean (S.D.)</td>
<td>Mean (S.D.)</td>
<td>Mean (S.D.)</td>
<td>Mean (S.D.)</td>
</tr>
<tr>
<td>PRM mean correct latency</td>
<td>2738(777.6)</td>
<td>3189.9 (1220.7)</td>
<td>2214.9 (578.2)</td>
</tr>
<tr>
<td>PRM number correct</td>
<td>19.8(3)</td>
<td>19.5 ( 2.6)</td>
<td>19.6(3.4)</td>
</tr>
<tr>
<td>PRM percent correct</td>
<td>82.7 (12.5)</td>
<td>81.2 (11)</td>
<td>81.9(14.2)</td>
</tr>
<tr>
<td>PAL first trial memory score</td>
<td>15.6 (4.6 )</td>
<td>15.9 (4.3)</td>
<td>18.1(4.4)</td>
</tr>
<tr>
<td>PAL Mean errors to success</td>
<td>3.7(2.7)</td>
<td>3.9 (3)</td>
<td>2.3 (2.5)</td>
</tr>
<tr>
<td>PAL Mean trials to success</td>
<td>2.1 (0.7)</td>
<td>2.2 (0.7)</td>
<td>1.7 (0.7)</td>
</tr>
<tr>
<td>* PAL Number of patterns succeeded on</td>
<td>7.1 (1.6)</td>
<td>7.2 (1.6)</td>
<td>7.5 ( 1.2)</td>
</tr>
<tr>
<td>PAL Stages completed on first trial</td>
<td>5 (1.2)</td>
<td>5.1 (1.1)</td>
<td>5.7 (1.3)</td>
</tr>
<tr>
<td>PAL Total errors</td>
<td>26.8(17.6)</td>
<td>28.6(20.7)</td>
<td>17.6(16.8)</td>
</tr>
<tr>
<td>PAL Total trials</td>
<td>16.3(4.6)</td>
<td>16.7(4.9)</td>
<td>13.5(4.2)</td>
</tr>
</tbody>
</table>

* We used Mann Whitney U Test for this variables(did not have normal distribution)

SOC, SST, and IED tests were used to assess the executive function. There was no significant
difference between the two groups in the SOC, SST, and IED test. The executive function scores
(SOC and IED tests) are presented in Table 4.
Table 4. Executive function variables (SOC and IED test) at baseline and retest in the two groups.

<table>
<thead>
<tr>
<th></th>
<th>Baseline CRT group</th>
<th>n=31</th>
<th>Mean (S.D.)</th>
<th>Baseline control group</th>
<th>n=31</th>
<th>Mean (S.D.)</th>
<th>Retest CRT group</th>
<th>n=28</th>
<th>Mean (S.D.)</th>
<th>Retest control group</th>
<th>n=28</th>
<th>Mean (S.D.)</th>
<th>Statistics</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>* SOC Mean initial thinking time (2 moves)</td>
<td>1591.2(1905.3)</td>
<td>n=31</td>
<td>Mean (S.D.)</td>
<td>1431.8(21252)</td>
<td>n=31</td>
<td>Mean (S.D.)</td>
<td>789 (718.8)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>1361.4 (1801.7)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>ANCOVA</td>
<td>0.570</td>
</tr>
<tr>
<td>* SOC Mean subsequent thinking time (2 moves)</td>
<td>375.2 (872.2)</td>
<td>n=28</td>
<td>Mean (S.D.)</td>
<td>630 (1697)</td>
<td>n=28</td>
<td>Mean (S.D.)</td>
<td>395.9 (814.4)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>273.6 (831.6)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>p-value</td>
<td>0.352</td>
</tr>
<tr>
<td>SOC Problems solved in minimum moves</td>
<td>6.1 (1.5)</td>
<td>n=31</td>
<td>Mean (S.D.)</td>
<td>6.2 (1.9)</td>
<td>n=31</td>
<td>Mean (S.D.)</td>
<td>7.1 (3.4)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>6.5 (2.4)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>0.591</td>
<td></td>
</tr>
<tr>
<td>IED Completed stage errors</td>
<td>17.9 (12.4)</td>
<td>n=28</td>
<td>Mean (S.D.)</td>
<td>13 (7.5)</td>
<td>n=28</td>
<td>Mean (S.D.)</td>
<td>12.9 (9.2)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>15.6 (10.4)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>0.334</td>
<td></td>
</tr>
<tr>
<td>IED Completed stage trials</td>
<td>82.3 (27)</td>
<td>n=28</td>
<td>Mean (S.D.)</td>
<td>69.1 (20.4)</td>
<td>n=28</td>
<td>Mean (S.D.)</td>
<td>69.8 (22.6)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>77.3 (23.8)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>0.262</td>
<td></td>
</tr>
<tr>
<td>IED EDS errors</td>
<td>12 (10)</td>
<td>n=28</td>
<td>Mean (S.D.)</td>
<td>15.5 (11.6)</td>
<td>n=28</td>
<td>Mean (S.D.)</td>
<td>13.1 (11.2)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>11 (10.3)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>0.262</td>
<td></td>
</tr>
<tr>
<td>IED Pre-ED errors</td>
<td>9.1 (6.6)</td>
<td>n=28</td>
<td>Mean (S.D.)</td>
<td>8.2 (4.8)</td>
<td>n=28</td>
<td>Mean (S.D.)</td>
<td>7.6 (4.1)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>10 (10.7)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>0.262</td>
<td></td>
</tr>
<tr>
<td>IED Total errors</td>
<td>25.5(16.7)</td>
<td>n=28</td>
<td>Mean (S.D.)</td>
<td>25 (10.4)</td>
<td>n=28</td>
<td>Mean (S.D.)</td>
<td>23 (13.4)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>25.1 (14.6)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>0.342</td>
<td></td>
</tr>
<tr>
<td>IED Total trials</td>
<td>96.8 (30.6)</td>
<td>n=28</td>
<td>Mean (S.D.)</td>
<td>92.1(17.1)</td>
<td>n=28</td>
<td>Mean (S.D.)</td>
<td>88.3 (21.9)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>95.2 (25.7)</td>
<td>n=28</td>
<td>Mean(S.D.)</td>
<td>0289</td>
<td></td>
</tr>
</tbody>
</table>

* We used Mann Whitney U Test for this variables (did not have normal distribution)

In summary, in this study, we did not observe any significant improvement in attention and executive function by using short-term computer-based CRT in patients with schizophrenia spectrum disorders. We observed only negligible to medium effects (as assessed by Cohen’s d) in some aspects of visual memory in patients who received CRT compared to standard treatment.

3. 5 Clinical and psychological outcomes

The secondary outcomes in this study were social functioning and psychopathology. The improvement in the global function, social functioning, and quality of life was compared between the two groups. Outcome measures are reported in Table 5.
Table 5. Clinical and psychological assessment in the two groups

<table>
<thead>
<tr>
<th></th>
<th>Baseline CRT group n=31</th>
<th>Baseline control group n=31</th>
<th>Retest CRT group n=28</th>
<th>Retest control group n=28</th>
<th>ANCOVA p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAF</td>
<td>6.5(1)</td>
<td>6.1(0.87)</td>
<td>6.8(1.2)</td>
<td>6.1(0.77)</td>
<td>0.034</td>
</tr>
<tr>
<td>CGI</td>
<td>2.1(0.86)</td>
<td>2.4(0.79)</td>
<td>1.8(0.77)</td>
<td>2.1(0.61)</td>
<td>0.034</td>
</tr>
<tr>
<td>PANSS Total</td>
<td>45.2(3.8)</td>
<td>45.9(3.8)</td>
<td>42.7(5.4)</td>
<td>44.2(5.1)</td>
<td>0.380</td>
</tr>
<tr>
<td>Positive symptoms</td>
<td>9.1(1.8)</td>
<td>9.9(3.6)</td>
<td>9(1.8)</td>
<td>9.5(2.6)</td>
<td>0.870</td>
</tr>
<tr>
<td>Negative symptoms</td>
<td>9.8(2.5)</td>
<td>9.8(1.9)</td>
<td>9.1(2.6)</td>
<td>9(2.1)</td>
<td>0.515</td>
</tr>
<tr>
<td>General psychopathology</td>
<td>26.6(2.4)</td>
<td>26.2(2.9)</td>
<td>24.9(3.2)</td>
<td>25.8(3.3)</td>
<td>0.121</td>
</tr>
<tr>
<td>QOL Q1</td>
<td>3.3(0.83)</td>
<td>3.1(1)</td>
<td>3.6(0.83)</td>
<td>3.4(0.92)</td>
<td>0.736</td>
</tr>
<tr>
<td>QOL Q2</td>
<td>3.3(0.86)</td>
<td>3.2(1.2)</td>
<td>3.4(0.97)</td>
<td>3.2(1)</td>
<td>0.519</td>
</tr>
<tr>
<td>Physical health</td>
<td>2.8(0.59)</td>
<td>2.8(0.54)</td>
<td>3(0.52)</td>
<td>2.9(0.40)</td>
<td>0.436</td>
</tr>
<tr>
<td>Psychological</td>
<td>2.9(0.64)</td>
<td>2.9(0.61)</td>
<td>3(0.64)</td>
<td>3(0.58)</td>
<td>0.636</td>
</tr>
<tr>
<td>Social relationships</td>
<td>2.4(0.93)</td>
<td>2.8(0.95)</td>
<td>2.5(1)</td>
<td>3(0.84)</td>
<td>0.031</td>
</tr>
<tr>
<td>Environment</td>
<td>3(0.91)</td>
<td>3(0.76)</td>
<td>3.1(0.92)</td>
<td>3.1(0.59)</td>
<td>0.140</td>
</tr>
</tbody>
</table>

* We used Mann Whitney U Test for this variables (did not have normal distribution)

** We used t test for this variable (did not meet assumptions required for ANCOVA)
There was statically significant difference in GAF (Z= -2.125, P= 0.034) and CGI (Z= -2.119, P= 0.034). There was no statically significant difference in PANSS (positive, negative, and general psychopathology scales) between the two groups after the termination of the study. In the assessment by the WHO QoL-Bref, there was a statically significant difference in the social relationships domain (F= 5.239, P=0.031).

4. Discussion

This study aimed to identify the role of short-term computer-assisted CRT on cognitive improvement in patients with schizophrenia spectrum disorders in a developing country. Due to limited resources, and according to our literature review, we provided the minimum number of CRT sessions. We used Cogpack software to improve three cognitive domains including attention, visual memory, and executive functions.

In this study attention and executive function were not improved by ten sessions of a CRT program. Some tasks of Cogpack software are trainer dependent, and training is influenced by trainer capabilities, motivation, and personality characteristics (Bowie, 2019). Nonetheless, a modest improvement in some scores of visual memory was detected which was not directly trainer dependent. Therefore, the results of this study should be interpreted with caution. Although this is a limitation, it is an advantage too. Providing services by different trainers is similar to the provision of services in the community. These findings were consistent with some previous studies (Dickinson et al., 2009), (Keefe & Harvey, 2012), (Rass et al., 2012), (Murthy et al., 2012), (Berry & Haddock, 2008).

Besides, we assessed the effect of computer-assisted CR on global functioning, clinical symptoms, and quality of life. This study supports the effects of CRT on global performance improvement and Clinical Global Impression (CGI). Our findings in the GAF test were consistent with the study of Sánchez et al (Sánchez et al., 2014). We did not find a significant change in the reduction of PANSS scores. Our results in clinical symptoms were consistent with a systematic review (Glenthøj, Hjorthøj, Kristensen, Davidson, & Nordentoft, 2017). As some literature suggests, cognitive impairment in these patients may affect their real-world functioning and quality of life (Bell, Bryson, & Wexler, 2003). Furthermore, cognitive deficits might be related to negative symptoms (Heydebrand et al., 2004). So the improvement in memory and executive function
domains of cognition may improve negative symptoms (Cella, Preti, Edwards, Dow, & Wykes, 2017). As mentioned before, we observed only a modest improvement in some scores of visual memory (mean trial to success, number of patterns succeeded, stages completed on the first trial, total trial). Our results did not support any significant improvement in cognition. Therefore, we observed no improvement in negative symptoms.

At the end of this study, we observed statistically significant improvement in only the social relationships domain of quality of life. A study proposed prolonged cognitive rehabilitation may impose improvement in the quality of life (Cavallaro et al., 2009). Maybe the duration of our study was not enough to create any improvement in the quality of life. The improvement in the social domain of quality of life may be created by social interaction and communication with health care providers in the treatment process.

The results of the current study did not support the conclusion of some previous studies (McGurk et al., 2007), (d’Amato et al., 2011), (Thorsen, Johansson, & Løberg, 2014), (Iwata et al., 2017). Several factors may contribute to these differences. Although some reviews confirmed the efficacy of 24-36 sessions of CRT in schizophrenia (Dickinson et al., 2009), (Bellack, Dickinson, Morris, & Tenhula, 2005), we provided the minimum rehabilitation sessions based on limited financial resources in our country. Maybe this intensity was not suitably efficient to create small to medium effects size as seen in the review of Wykes et al, 2011 (Wykes, Huddy, Cellard, McGurk, & Czobor, 2011).

In this study, CRT was the only psychosocial intervention that was provided to the patients. Most literature suggests that CRT should be integrated into a comprehensive rehabilitation program to create the greatest effect size compared with CRT alone (Wykes et al., 2011), (McGurk et al., 2013), (Bowie, 2019).

Strengths and Limitations

We had some limitations in this study. The long-term effect of the intervention; was not investigated, and we did not follow the results after the termination of CRT sessions. The findings may be influenced by the small sample size and short duration of the intervention. Because of the software design and using the English language, the role of education status was prominent. We did not use some tools of the English version of Cogpack software based on patient difficulty
incomprehension. Therefore, most of our patients were dependent on the trainer to understand the task instructions. The intervention was provided by different therapists with different levels of motivation and interests, personality traits, and teaching skills which can cause difficulties in the interpretation of our results. Furthermore, there was no specific indicator to evaluate the qualification of supervision sessions.

There are also some strengths in this study. We used a computer-based cognitive battery to assess cognitive function and also computer-based cognitive remediation (CCR) program to improve cognitive performance. Therefore, the role of subjective influence would be limited.

In our study, cognitive performance in some domains was decreased, and participants feel anxious receiving feedback. This could affect their performance. Providing feedback only in cases of cognitive improvement could be a solution.

**Future Directions:**

We did not observe significant improvements in patients’ cognitive functioning and overall performance after a short course CRT as an independent psychological intervention. This intervention should be integrated into a comprehensive rehabilitation program for these patients. Employing well-trained and motivated therapists along with planning for regular supervision sessions, using more interesting visual tasks, holding more rehabilitation sessions in prolonged duration, and providing this intervention in the early phase of the illness is recommended. Based on the language and cultural issues, these software packages should be adapted. The authors also suggest conducting a Persian version of the Cogpack software for the Iranian population.

**Acknowledgement**

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**Conflict of Interest**

None.
References:


