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The Effect of a Computer-Assisted Cognitive Remediation on Improving Cognitive Functions in Patients with Schizophrenia: A Before-After Study

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Abstract

Background: Cognitive impairment is a chronic and disabling manifestation of schizophrenia.

Objectives: This before-after study was conducted to examine the effect of a short course computer-assisted cognitive remediation on improving cognitive functions of patients with schizophrenia.

Materials and Methods: Twenty patients with schizophrenia were enrolled into the study. The intervention consisted of 10 one-hour sessions held 2-3 times a week, using the Cogpack software that includes tasks to improve attention, memory, and executive function. The patients' cognitive functioning was assessed before and after the remediation, using tests in the CANTAB battery, including stop signal task (SST) and choice reaction time (CRT) to assess attention levels, pattern recognition memory (PRM) and Paired associate learning (PAL) to examine memory, and stocking of Cambridge (SOC) and intra-extra dimensional task (IED) to evaluate executive function.

Results: IED and SOC revealed a statistically significant improvement in executive function after the intervention. PAL revealed a significant improvement in memory functioning in most aspects after the intervention, while PRM did not. CRT showed a significant improvement in some aspects of attention and concentration after the intervention, while SST did not.

Conclusions: This before-after study revealed that a relatively short course of a computer-assisted cognitive remediation can be applied to improve several aspects of cognitive functioning in patients with schizophrenia. A randomized controlled trial is required to establish the effectiveness of the intervention.

Keywords: Cognitive, Rehabilitation, Schizophrenia

1. Background

Cognitive impairment is a chronic and disabling manifestation of schizophrenia. Functional achievement of the patients with psychotic disorders is reported to be less than 85% of the general population's scores in cognitive tests (1). Thus, cognitive impairment persists even after the patient is clinically stable; on the other hand, medications do not significantly improve cognitive impairments in schizophrenia (2). Although they can improve attention through reducing psychotic symptoms, the residual attentional problems after the amelioration of psychotic symptoms are usually treatment-resistant, and can be observed throughout the course of illness (2).

The main cognitive domains that are disturbed in schizophrenia include executive function, attention, verbal memory, psychomotor coordination, and learning abilities. Cognitive remediation (rehabilitation) is a method used to improve cognitive functions and quality of life in patients with schizophrenia, and is considered a behavioral treatment for cognitive impairments that disturb patients' everyday activities. For the first time, Brenner et al. (3) developed a comprehensive therapy plan for cognitive remediation of patients with schizophrenia in 1994. Since then, several studies have examined its efficacy; a review of the recent research reveals that most of them compared cognitive remediation with other rehabilitation methods, or cognitive behavioral treatments (4). In most of the studies, rehabilitation was applied via computer-assisted techniques over one to six months. Patients with the DSM-IV schizophrenia were evaluated in terms of cognitive functions before, during, and after the study in variable follow-up periods. The findings of most of these studies confirm the effectiveness of cognitive rehabilitation on the general and cognitive functioning of the patients (5).

Although many studies have been conducted on this topic around the world, only one study was done in Iran (6) that investigated the efficacy of Sholberg cognitive-remediation therapy. However, this study was not computer-assisted. It is noteworthy to mention that computerized cognitive remediation provides a standard

condition to instruct all the patients, and results in more accurate measurements. In addition, if we can employ an effective remediation program in a short course, its application in clinical settings would be much easier and less costly.

2. Objectives

This study was conducted to assess the effect of a relatively short course computer-assisted cognitive remediation therapy on several aspects of cognitive functioning, including attention, memory and executive function, in patients with schizophrenia, using a standardized assessment battery.

3. Materials and Methods

3.1. Participants

Twenty patients with DSM-IV schizophrenia aged 18 to 55, residing in Tehran who referred to Roozbeh hospital were enrolled, using a convenience sampling procedure. The diagnoses were ascertained by an attending psychiatrist and confirmed by administering the structured clinical interview for DSM-IV (SCID), Persian version. Patients were in a stable clinical condition at the time of enrolment, and written informed consents were obtained from patients' guardians. The exclusion criteria are as follows: Educational level lower than 8th grade, receiving ECT during six weeks prior to the study, mental retardation, visual impairment, concurrent consumption of substances with the exception of nicotine and caffeine, a history of head trauma followed by loss of consciousness, concurrent consumption of anticonvulsant medications (due to their adverse effects on cognitive functions), and suffering from major neurologic disorders including epilepsy, Parkinson's disease, dementia, multiple sclerosis, and any motor disability. The dosage and the type of antipsychotic medications that the patients were receiving at least during the three weeks prior to the study were stable. Due to the adverse effects of benzodiazepine on cognition and psychomotor performance, the patients received their last dose of a benzodiazepine (if any) at least 12 hours before the intervention, but no antihistamine medication was administered.

3.2. Intervention

The cognitive remediation protocol consisted of 10 sessions of computerized training, using the Cogpack software (7). This software includes a range of tasks to improve attention, memory, and other cognitive functions. The tasks were selected from different aspects, including distributive attention, selective attention, short-term memory, working memory, long-term memory, sustained attention, planning and problem solving, and recognition of rules and patterns. The tasks were divided into three levels: Easy, moderate (4th to 8th sessions), and difficult. This study included 21 tasks in total, including new-or-not, logic, borders, route, ball, maze, on the road, reaction time, comparisons, search, memory, scan, piecework, multiplication, math A, math B, visual motion, confusion, sequence, unidentified flying objects (UFOs), and eyewitness.

Overall, out of 20 patients, two participated in seven sessions of therapy (one stopped following the treatment and one was suggested to receive ECT by the treating physician), 16 attended 10 sessions, and two attended 11 sessions due to the long interval between the second and the third sessions.

3.3. Measures

Positive and negative syndrome scale (PANSS) was used to investigate psychotic symptoms. Several studies confirmed the reliability of this scale (8). Clinical global impression (CGI) was used for clinical evaluation of the patients in terms of illness severity upon entering the study. Global assessment of functioning (GAF) was employed to assess global functioning of the patients. The scale has shown adequate reliability and validity indices (9). Five subscales of the adult Wechsler test were used to measure the baseline IQ of the patients; i.e., digit symbols, similarities, block design, vocabulary, and comprehension. Furthermore, illness and treatment history was obtained, using chart reviews as well as interviews with patients and their relatives.

The CANTAB software (Cambridge Neuropsychological Test Automated Battery) (10) was employed to assess the cognitive functioning before and after intervention and includes simple and computerized tests that are independent of language and individual cultural differences, and are administered by a trained assistant and a therapist. These tests can easily provide interpretation for the cases. Before and after remediation, we assessed attention using Stop Signal Task and Choice Reaction Time, memory using pattern recognition memory and paired associate learning test, and executive function using Stocking of Cambridge test and Intra-Extra Dimensional task.

3.4. Procedures

Diagnosis of schizophrenia was ascertained by the attending psychiatrists in Roozbeh hospital. Before remediation, the IQ level of the patients was assessed by a Master's degree in psychology, using the adult Wechsler intelligence scale (WAIS) (11). In addition, all the participants

were evaluated for psychotic symptoms and functioning, using positive and negative syndrome scale (PANSS) and global assessment of functioning scale (GAF), respectively prior to the intervention. Cognitive remediation was preformed if the patients were clinically stable and not acutely psychotic (CGI < 4; PANSS < 50). To examine the stability of clinical condition, both CGI and GAF were administered again after the intervention. During the intervention, the patients received their medications as they were prescribed before, but in case the symptoms became severe or there was a need to change the type of medication or its dosage, the patient was excluded from the study.

The intervention consisted of 10 one-hour sessions held 2 - 3 times a week (three times a week for the inpatients and two times a week for outpatients), using the Cogpack software. On average, the intervention lasted for one month. Rehabilitation was performed individually and under the supervision of a Master's degree in psychology in a quite setting, and during the same time of the day in the morning for each patient. During the intervention, the instructions for performing the tasks were explained to the patients. Attention, memory, and executive function were assessed both before and after the intervention, using the relevant CANTAB tests. Both the intervention and the assessments were conducted in Roozbeh hospital. The assessments were conducted at the intervals of 2 - 5 days before and after the intervention. PRM, PAL, SOC and IED tests in the CANTAB software were performed first; then CRT and SST tests were given after a 15-minute break.

All aspects of the Declaration of Helsinki were observed. The patients' demographic information was kept confidential, and written informed consent was obtained from all patients before entering the study. All the procedures of the study were fully and clearly explained to the patients. The patients were free to withdraw from the study if they were not willing to continue. Outpatients received transportation fares to and from the hospital.

All the analyses were performed, using the SPSS software, Version 20. Paired t- test was used for the before-after comparisons, and p value was set at 0.05.

4. Results

Out of 20 participants, 16 (80%) were male. The mean age of the patients was 35.5 years (SD = 8.3), and the mean duration of the illness was 135.3 months (SD = 93.4). With respect to educational level, 1 (5%) had an 8th grade education, 1 (5%) a 10th grade education level, 11 (55%) held a high school diploma, and 7 (35%) a college or university degree. One patient (5%) was married and 19 (95%) were single. Three patients (15%) were employed, 15 (75%) unemployed, and 2 (10%) disabled. Six patients (30%) took typical antipsychotic medicine, six (30%) were treated with atypical antipsychotic medicine, and eight (40%) received both typical and atypical antipsychotic drugs.

The dosages of different medications were converted to equivalent haloperidol (for typical antipsychotic), or risperidone (for atypical antipsychotics). The minimum dosage of the typical antipsychotic drug (haloperidol equivalent) taken by the patients was 0.8 mg, the maximum was 42 mg, and the average was 19.6 mg (SD = 15.2). The minimum dosage of the atypical antipsychotic drug (risperidone equivalent) taken by the patients was 2 mg, the maximum was 10.5 mg, and the average was 5.3 mg (SD = 2.7). The minimum GAF was 56, the maximum was 83, and the average was 67.2 (SD = 7.9). The minimum CGI was 2, the maximum was 3, and the average was 2.7 (SD = 0.4). Patients' clinical conditions were stable during the intervention as reflected in almost unchanged average GAF and CGI after the intervention (67.5 [SD = 7.5] and 2.6 [SD = 0.5], respectively).

SOC test was used to assess the executive function both before and after rehabilitation. A significant difference was observed before and after rehabilitation in all the three scales (Table 1). Table 2 displays the executive function (set shifting) before and after rehabilitation. Paired t-test revealed significant improvements in both scales of executive function in patients with schizophrenia.

PRM and PAL tests were utilized to assess visual memory. Tables 3 and 4 demonstrate the results of these tests.

Paired t-test revealed a significant difference in three scales out of four. As demonstrated in Table 4, no significant improvement was observed, but the rate of improvement of mean correct latency was 5.5%. Table 5 displays the results of the assessment of attention and impulsivity (attention and speed of response to stimulus) before and after rehabilitation, using the CRT test. The results of the t-test indicated a significant difference before and after intervention just in two scales: The percent correct trials and mean correct latency.

SST test was used to assess attention and impulsivity (inhibition and impulsivity) before and after rehabilitation; the results are reported in Table 6. As shown, no significant difference was observed in any of the scales.

5. Discussion

The assessment of executive function revealed that both IED and SOC tests showed a significant improvement in most domains after the intervention. PAL test that assesses memory showed a significant improvement in most domains after the intervention, while PRM test did not show such a difference. With regards to attention and concentration, CRT test revealed some significant differences

Table 1. Comparison of the Stocking of Cambridge (SOC) Test Results Before and After Intervention in Patients with Schizophrenia (n = 20) Participating in a Cognitive Remediation Program, using the Cogpack Software

SOC	Before, Mean (SD)	After, Mean (SD)	t	P Value	Improvement (%)
Mean initial thinking time (2 moves) (ms)	1707.52 (1754.67)	1159.50 (1500.76)	2.36	0.02	32.1
Mean subsequent thinking time (2 moves) (ms)	854.57 (1523.12)	141.51 (386.52)	2.25	0.03	83.4
Problems solved in minimum moves	6.90 (1.37)	7.80 (1.47)	-2.43	0.02	13.0

Table 2. Comparison of the Intra-Extra Dimensional Set Shifting (IED) Test Results Before and After Intervention in Patients With Schizophrenia (n = 20) Participating in a Cognitive Remediation Program, Using the Cogpack Software

IED	Before, Mean (SD)	After, Mean (SD)	T	P Value	Improvement (%)
Completed stage errors	10.05 (5.08)	7.00 (3.15)	3.40	0.003	30.3
Completed stage trials	70.45 (9.37)	63.30 (7.02)	2.96	0.008	10.1
EDS errors	2.95 (2.68)	1.20 (1.47)	2.88	0.009	59.3
Pre-ED errors	6.45 (3.58)	4.55 (1.64)	2.28	0.03	29.5
Total errors	10.95 (5.08)	7.00 (3.15)	3.40	0.003	36.1
Total trials	70.45 (9.37)	63.30 (7.02)	2.96	0.008	10.1

Table 3. Comparison of the Paired Associated Learning (PAL) Test Results Before and After Intervention in Patients With Schizophrenia (n=20) Participating in a Cognitive Remediation Program Using the Cogpack Software

PAL	Pretest, Mean (SD)	Posttest, Mean (SD)	t	P Value	Improvement (%)
First trial memory score	15.40 (4.38)	17.10 (4.23)	-1.35	0.19	11.0
Mean errors to success	3.73 (2.62)	2.21 (1.54)	2.37	0.02	40.8
Mean trials to success	2.10 (0.62)	1.71 (0.42)	2.28	0.03	18.6
Number of patterns succeeded on	7.70 (0.73)	8.00 (0)	-1.83	0.08	3.9
Stages completed	7.85 (0.37)	8.00 (0)	-1.83	0.08	1.9
Stages completed on first trial	4.90 (1.07)	5.50 (1.00)	-1.55	0.13	12.2
Total errors	28.70 (18.94)	17.75 (12.31)	2.34	0.03	38.2
Total trials	16.35 (4.15)	13.75 (3.34)	2.18	0.04	15.9

Table 4. Comparison of the Pattern Recognition Memory (PRM) Test Results Before and After Intervention in Patients With Schizophrenia (n = 20) Participating in a Cognitive Remediation Program Using the Cogpack Software

PRM	Pretest, Mean (SD)	Posttest, Mean (SD)	T	P Value	Improvement (%)
Mean correct latency	2936.13 (1048.03)	2774.29 (888.04)	0.97	0.34	5.5
Number correct	19.90 (2.20)	19.65 (2.91)	0.35	0.72	-1.3
Percent correct	82.91 (9.16)	81.87 (12.11)	0.35	0.72	-1.3

in some aspects after the intervention, while SST test did not show such a difference. The rate of improvement after the intervention was 13% - 47% for SOC, 10% - 59% for IED, 11% - 57% for PAL, 5.5% for PRM, and 75% - 80% for CRT. This study did not have a control group; therefore, we could not rule out the placebo effect of the intervention in the observed improvements.

Improvements were observed in some aspects of attention. The results of the tests showed a significant improvement in just two of the aspects in CRT test. Since CRT and SST were almost similar and each lasted 15 - 20 minutes, one of the reasons for which SST did not show any significant difference in the results was that it was carried out immediately after CRT.

Table 5. Comparison of the Choice Reaction Time (CRT) Test Results Before and After Intervention in Patients With Schizophrenia (n = 20) Participating in a Cognitive Remediation Program, Using the Cogpack Software

CRT	Pretest, Mean (SD)	Posttest, Mean (SD)	t	P Value	Improvement (%)
Percent commission trials	0.20 (0.62)	0.05 (0.22)	1.00	0.32	75.0
Percent correct trials	98.05 (2.80)	99.40 (0.99)	-2.52	0.02	1.4
Percent omission trials	0.25 (0.91)	0.05 (0.22)	0.94	0.35	80.0
Mean correct latency	555.12 (146.43)	484.70 (115.15)	2.08	0.05	12.7
Total commission errors	0.55 (2.04)	0.05 (0.22)	1.08	0.29	90.9
Total omission errors	0.25 (0.91)	0.05 (0.22)	0.94	0.35	80.0

Table 6. Comparison of the Stop Signal Test (SST) Test Results Before and After Intervention in Patients With Schizophrenia (n = 20) Participating in a Cognitive Remediation Program Using the Cogpack Software

SST	Pretest, Mean (SD)	Posttest, Mean (SD)	t	P Value	Improvement
Direction errors on stop and go trials	3.95 (8.59)	1.50 (1.85)	1.21	0.23	-62.0
Proportion of successful stops(last half)	0.57 (0.15)	0.55 (0.11)	0.67	0.50	-3.5
Median correct RT on GO trials	878.45 (243.68)	838.52 (141.00)	0.70	0.49	-4.5
SSD (50%)(last half)	571.03 (150.82)	579.76 (110.54)	-0.25	0.79	1.5
SSRT (last half)	307.41 (125.98)	257.40 (79.93)	1.51	0.14	16.3

Moreover, improvements were observed in short-term memory, long-term memory, and working memory. The assessment of memory, using PAL and PRMs, revealed a significant difference in only four aspects on PAL test. This finding is in line with a study conducted by Prouteau et al., 2005 (12). However, this study did not find a significant difference in the results of PRM before and after intervention. A study done by Jennifer Barnett et al., 2007 (13), indicated that the results of PRM did not suggest a positive change toward improvement as time went by. Furthermore, Immanuel Stip et al., 2008 (14), reported some heterogeneous effects on PRM percent correct, while they were assessing visuo-spatial cognition in patients with schizophrenia. On the other hand, non-significant differences can be interpreted as the fact that PRM involves automatic aspects of cognitive function that are not disturbed as much as non-automatic aspects in schizophrenia (15).

Some other aspects investigated in this study were planning and problem solving and recognition of rules and patterns. These aspects were assessed by SOC and IED tests. The results revealed a significant improvement in three scales in SOC and in two scales in IED. The significant difference in SOC is in line with the findings of the study conducted by Antoni Prouteau et al., 2005 (12).

Expert reviews from six meta-analyses have revealed strong support for moderate (approximately 0.5 SD) improvements on measures of neurocognitive function distinct from the tasks trained as part of specific remediation protocols, and these effects generalize to function (5). This study was conducted without including other rehabilitating interventions. Therefore, maximum improvement in cognition should not be expected since as time goes by after the diagnosis of the disease and the prescription of the drugs (2), no improvement will be expected in patients' cognition without cognitive remediation. Moreover, no change was detected in the dosage of the drugs taken by the patients in this study, so it is far from expectation to attribute the cognitive improvement to the increased dosage of the drugs. Thus, considering the stability in the patients' mental condition (comparing the scores of GAF and CGI before and after the intervention); it seems that cognitive improvement can be due to cognitive remediation.

A significant difference was found in most aspects of cognition, including executive function, memory, attention, and concentration after a relatively short course of cognitive remediation. The results of this study are in line with most other studies (16, 17), particularly the study by Prouteau et al., 2005 (12). We provided a relatively short course of remediation that would be more practical and less costly, especially in less developed or resourceful settings.

Among limitations of this study were the lack of a control group and small sample. Some other limitations were lack of follow-up to assess the patients' cognition over a few months after the intervention, and not using all the tools of the Cogpack software for training since our pa-

tients did not comprehend English.

It is recommended that cognitive remediation be combined with other non-medical treatments, such as occupational therapy and social skills training to obtain more effective results and to test its effectiveness, using a randomized controlled design.

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Footnotes

Authors' Contribution: Vandad Sharifi conceived and designed the evaluation. Azadeh Sedighnia collected the clinical data. Vandad Sharifi performed the statistical analysis. Vandad Sharifi and Azadeh Sedighnia interpreted the clinical data. Azadeh Sedighnia and Shima Ataie drafted the manuscript. Vandad Sharifi revised it critically for important intellectual content. Vandad Sharifi and Azadeh Sedighnia did the administrative, technical, and material support. Vandad Sharifi, Mehdi Tehranidoost and Maryam Tabatabaee supervised the study. All authors read and approved the final manuscript.

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