



# The Effectiveness of Computer-Based Cognitive Rehabilitation in Executive Functions in Patients with Multiple Sclerosis

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## Abstract

**Background:** Multiple sclerosis (MS) is a common chronic disease of the nervous system. A problem facing MS patients is cognitive impairments, including executive functions as the most major deficiency.

**Objectives:** The present study was conducted to investigate the effectiveness of cognitive rehabilitation in executive functions in MS patients.

**Methods:** The present controlled quasi-experimental study was conducted on a population comprising all MS patients who were members of the MS Society in Kermanshah, Iran using a pretest-posttest approach. The computerized form of Wisconsin card sorting test (WCST) was administered on 60 patients, of whom 20 were selected and randomly assigned to an experimental group (n = 10) and a control group (n = 10). The experimental group participated in twelve 50-minute sessions of computer-based cognitive rehabilitation intervention, whereas the controls did not undergo any interventions. After completing the intervention, the post-test was performed in both groups, and the data were analyzed using ANCOVA.

**Results:** The findings suggested significant statistical differences ( $P < 0.001$ ) in the posttest results of the patients' performance compared to the pretest stage in the experimental and control groups.

**Conclusions:** The findings obtained suggest that cognitive rehabilitation improves executive functions in MS patients. This method is recommended to be used in rehabilitation centers and psychological clinics to improve cognitive problems in MS patients.

**Keywords:** Computer-Based Cognitive Rehabilitation, Multiple Sclerosis (MS), Executive Functions

## 1. Background

Multiple Sclerosis (MS) is a chronic immune-mediated disease causing inflammation, demyelination and neurodegeneration of the central nervous system (CNS) (1). The clinical symptoms of the disease are varied, depending on the location of plaques or lesions within the CNS, but can include both physical difficulties and also cognitive difficulties. Although the physical limitations of living with MS have been extensively documented, the details of MS-associated cognitive disorders in patients outside specialized clinics have rarely been addressed in literature (2). Approximately 43% - 70% of MS patients are affected by cognitive dysfunction. The main cognitive domains affected by this disease include attention, data processing, executive functions, memory and visuospatial abilities (3). Cognitive disorders are normally diagnosed in the course of MS, although they can be detected in the early stages of the disease emergence. Different studies reported the detection of cognitive disorders in the early stages of the disease in 26% - 54% of the patients. The primary symptoms

of this disease involve memory and attention, and particularly complicated functions requiring attention reveal this defect. Mild cognitive damage affects the habits and normal process of life in the patients. The most prevalent of these disorders include impaired abstract thinking, attention disorder, word retrieval, problem solving and visuospatial and memory disorders (4).

Executive functions are supreme cognitive and metacognitive functions that fulfil a collection of supreme abilities and help individuals in life with identity actions and performing learning-associated activities. In other words, these skills help an individual focus on important aspects of activities and plan for completing them (5). Research suggests that 15% - 20% of MS patients face difficulties with executive functions (6). These functions appear to involve several processing centers in different regions of the brain; yet, these are mainly located in the frontal lobe and pre-frontal cortex (7). These neurocognitive functions are major structures, which are practically associated with psychological processes responsible for controlling alertness and thinking (8), and considered a

collection of supreme abilities, including self-regulation, inhibition, self-initiation, strategic planning, abstract ability, cognitive flexibility and impulse control (9).

Today, neuropsychological therapies and cognitive rehabilitation methods are widely used to help patients. Cognitive rehabilitation constitutes a structured collection of therapeutic activities designed for memory retrieval and other cognitive functions based on evaluating and understanding patients' brain and behavioral disorders (10). Cognitive rehabilitation therapy is based on certain principles of neuroplasticity of the brain, and refers to purposeful exercises for improving different domains of cognition such as attention, memory, language and executive functions (11).

Recent two decades have witnessed remarkable advances in cognitive sciences, and paper-and-pencil tests have been supplanted by computerized tests in the field of evaluation and diagnosis (12). Computer-based cognitive rehabilitation in conjunction with conventional training is more effective than the merely conventional paper-and-pencil education (13). A study conducted in Iran confirmed the effectiveness of computer-based cognitive rehabilitation in improving executive functions in MS patients (14).

Investigating the effect of computer-based rehabilitation training on MS patients with attention deficit showed that specific rehabilitation training can cause higher improvements in attention compared to non-specific training (15). Neuropsychological rehabilitation was also found to affect attention, data processing and executive functions and improve depression in MS patients with low levels of disability (3).

## 2. Objectives

Research suggests the effectiveness of cognitive rehabilitation in improving cognitive functions. Given the cognitive problems of MS patients and the major role of cognitive functions such as executive functions in these patients as well as the inadequate number of studies addressing this subject, investigating the effectiveness of cognitive programs in improving executive functions appears essential. The present study was therefore conducted to determine whether or not computer-based cognitive rehabilitation improves executive functions and the speed of data processing in MS patients.

## 3. Methods

The present controlled quasi-experimental research used a pretest-posttest approach to study a population comprising all MS patients who were members of the MS society in the city of Kermanshah, Iran. Convenience sampling was used to select the subjects. To assess executive

functions, a computerized WCST was administered on 60 candidates, of whom 20 eligible patients with the lowest scores, i.e. perseverative error  $\leq 20$ , were selected and randomly divided into the experimental group ( $n=10$ ) and the control group ( $n=10$ ). The inclusion criteria consisted of an age of 18 - 45 years, reading and writing literacy and a willingness to participate in the study. The exclusion criteria comprised dementia and severe psychiatric disorder recorded in medical or psychiatric files, participation in other rehabilitation programs and severe motor disabilities interfering with the study process. The study patients were found to be acceptable in terms of the score of below 3.5 they received from the expanded disability status scale (EDSS), which is used for evaluating physical disabilities.

After selecting the study subjects, the rehabilitation program sessions were held in the experimental group based on the required protocol. The number and duration of each session were selected based on the study conditions. Twelve 50-minutes sessions of computer-based cognitive rehabilitation program were therefore individually held in the experimental group twice a week. In the meantime, the control group received no trainings. The WCST was conducted as the posttest ten days after the last session in both groups to determine the effect of the rehabilitation program.

The computerized WCST is used to measure executive function variables, and consists of 64 cards in different shapes and colors (16). This test was introduced by Grant and Berg (1948, according to Lezak, 1994). The validity of this test was reported to be over 86% for cognitive deficits caused by brain injuries, and its reliability to be 85% in an Iranian sample using the test-retest method (5). Four main cards in this test, including a red triangle, two green stars, three yellow crosses and four blue circles, are constantly displayed at the top of the monitor until the end of the test. Sixty other cards totally randomly appear one-by-one at the bottom of the screen close to the right hand corner. When a card is displayed, the subject should decide on the main card it should be placed under. Each of these 60 cards is presented only once, and none is used twice. In fact, when the first card is presented and the subject responds, it is discarded from the set of 60 cards, and the test continues with the remaining 59 cards. A review of literature suggests that ten items are normally scored as the output when the WCST is used; nevertheless, depending on the objectives in each study, a number of these items are considered the output, and all the ten items have rarely been considered by researchers. The vast majority of researchers in this field have proposed "number of completed or obtained categories" and "number of perseverative errors" as the main indicators of executive function evaluation (16).

The Captain's Log cognitive rehabilitation software (version 2014) is an educational collection for promoting

supreme functions and processes. This program was designed based on a basic data processing system, active memory and central processing speed. It therefore involves both basic and supreme cognitive skills. The Captain's Log system can evaluate an individual on nine domains of cognitive functions, and recommends a training program according to the individual's status. One can design a comprehensive program consistent with their abilities using this system. Such a program can also be designed and presented for an individual in a clinical setting, while other similar programs lack such capability. This program first helps improve basic skills, including visual and auditory processes, followed by presenting more difficult tasks and different levels of skills. The Captain's Log system offers advanced settings, and the therapist can cause individual abilities to be faced with more challenges in every stage of the exercise, so that the person can enhance his skills and also use his higher levels of potentially-unrecognized abilities.

### 3.1. Intervention Program

The present study used the Captain's Log software. Based on the variable of executive functions and its components, two programs were selected and administered, namely stimulus reaction/inhibition (red light and green light) and scanning reaction/inhibition (mouse hunt), each comprising 15 different stages. The closer the subjects to the end stages, the more difficult the stages. Entering the next stage required completing the previous task, and successfully completing these stages was equivalent to entering higher stages of the next sessions. The therapist carefully reviewed how each assignment was performed, and explained it for the experimental group in a simple and straightforward language. The program of each session was different from that of the previous session, which encouraged the subjects to continue their therapy (Table 1).

After collecting the data, their mean and standard deviation were determined, and the data obtained from the computerized WCST were analyzed in SPSS-24 using ANCOVA.

## 4. Results

The mean age of the experimental group was  $38.10 \pm 8.71$  years and that of the controls was  $36 \pm 6.35$  years, and these groups were matched in terms of age ( $P = 0.55$ ). Furthermore, the experimental group consisted of six women and four men, and the control group comprised five women and five men, and these groups were also matched in this respect ( $P = 0.65$ ).

Table 2 presents the pretest and posttest mean values of executive function components (the WCST) by group, suggesting that the mean of the component of number of categories reached a posttest value of 4.8 from a pretest value of 2.2 in the experimental group. The mean perseverative error also reached a posttest value of 3.80 from a pretest value of 9.90 in the experimental group. In addition, in this group, the mean pretest value of the total error reached 19 from a pretest value of 30.90, while the mean pretest value of other errors decreased from a pretest value of 21 to a posttest value of 19.50.

Table 3 presents the results of multivariate covariance analysis (MANCOVA) conducted to evaluate the effectiveness of cognitive rehabilitation in executive functions, suggesting that the tests are significant ( $P < 0.001$ ), and that the experimental and controls groups are significantly different at least in one of the dependent variables, i.e. executive functions. MANCOVA was used to identify in which component of the executive functions the difference is significant, and the results are presented in table 4.

Table 4 suggests that cognitive rehabilitation significantly affects every single component of the executive functions. Moreover, eta squared shows that this intervention exerts its maximum effect on the total error (0.88), as it was the highest in this component.

According to the analysis results, cognitive rehabilitation appears to significantly affect the executive functions, i.e. cognitive flexibility and inhibitory control.

## 5. Discussion

Cognitive dysfunction has been found to exert significantly negative effects on daily life of MS patients. MS patients with cognitive problems are reluctant to participate in the community and occupational activities, have a high unemployment rate, and present more difficulties in performing daily household chores. Developing and validating the therapeutic mechanisms of cognitive dysfunction is therefore crucial (17). In a controlled randomized trial, Hanssen et al. found cognitive rehabilitation to improve certain dimensions of life in MS patients (18). Another study investigated the effect of attention deficit retention in MS patients using AIXIENT, and found significant improvements in the attention function of the experimental group, and reported fewer attention-related problems in daily situations (19).

Creating experiences is widely believed to somehow improve posttraumatic functions in patients with brain traumas, and to change the brain's neuron development by preparing the designed experiences and therefore improving their daily living functions, which is called cognitive rehabilitation. Some researchers believe that cognitive rehabilitation can guide neuronal changes in certain

**Table 1.** The Therapeutic Protocol in Each Cognitive Rehabilitation Session Associated with Captain's Log

Program	Implementation Instructions	Skill Promotion
<b>Stimulus reaction/inhibition</b>	Images are randomly displayed at a time, and the subject should quickly decide whether the image is of the same color as the screen margin or not. Practicing this program increases the subject's self-control and mental processing	Intermittent attention; response inhibition; visual imaging; speed of visual processing; conceptual reasoning.
<b>Scanning reaction/inhibition</b>	An image is displayed on the screen. If the color of this image matches the color of the screen margin, the subject should quickly click, and should not do anything if it is different. This program has different stages, and this instruction is totally reversed in some stages	Intermittent attention; visual tracking; response inhibition; boosted attention; speed of visual processing

**Table 2.** The Pretest and Posttest Descriptive Indices of the Components of Executive Functions by Group<sup>a</sup>

Variable	Group			
	Experimental		Control	
	Pretest	Posttest	Pretest	Posttest
<b>Number of categories</b>	2.20 ± 1.23	4.80 ± 1.13	3.50 ± 1.18	3.50 ± 0.70
<b>Perseverative error</b>	9.90 ± 5.63	3.80 ± 2.74	7.20 ± 3.46	6.70 ± 1.70
<b>Total error</b>	30.90 ± 8.77	19 ± 4.39	27.90 ± 2.45	40.70 ± 2.45
<b>Other errors</b>	21 ± 4.92	15.20 ± 4.93	18.10 ± 3.25	19.50 ± 2.91

<sup>a</sup> Values are expressed as mean ± SD.

**Table 3.** Comparing the Experimental and Control Groups Using MANCOVA in the WCST

Test	Value	F	df (Hypothesis)	df (Error)	Significance Level	Etta Square
<b>Pillai's trace</b>	0.90	24.15	4	11	0.001	0.90
<b>Wilks' lambda</b>	0.10	24.15	4	11	0.001	0.90
<b>Hotelling trace</b>	8.78	24.15	4	11	0.001	0.90
<b>Roy's largest root</b>	8.78	24.15	4	11	0.001	0.90

**Table 4.** ANCOVA on Mean Values of the Components of Executive Functions

Dependent Variable	Sum of Squares	df	Mean Square	F	Significance Level	Etta Squared
<b>Number of categories</b>	11.43	1	11.43	12.88	0.003	0.48
<b>Perseverative error</b>	62.89	1	62.89	15.27	0.002	0.52
<b>Total error</b>	2152.73	1	2152.73	101.43	0.001	0.88
<b>Other errors</b>	103.30	1	103.30	5.97	0.03	0.30

circumstances (20). Neuroplasticity refers to the ability of the nervous system to respond to internal or external stimuli by identifying its own structure, function and communications. In fact, the brain can identify its structure and functional communications to maximize their capacities and adaptation to its own resources and confront cognitive deficits. The changes in functional activity have been often associated with improved cognitive functions such as cognitive rehabilitation in MS patients. Neuroplasticity has been recently used in many studies to explain the therapeutic effects of cognitive rehabilitation. Structural and functional neuroimaging have been found to be as-

sociated with improvements in cognitive abilities in cognitive rehabilitation therapy of MS. Cognitive deficits of MS have been found to be associated with different sizes of the brain regions such as the size of T2 lesion, cerebral atrophy, third ventricular width, cerebellum size and cortical lesions in cognitive studies on MS using neuroimaging. Moreover, the extensive application of functional neuroimaging techniques in the MS population has confirmed the changes in the patterns of brain activity and functional relationships (17).

The present study findings suggested no significant differences between the experimental and control group

in terms of the pre-intervention mean values of the executive functions, although the posttest values were significant. These results therefore confirm the effectiveness of cognitive rehabilitation intervention in executive functions, which is consistent with literature (3, 14, 18, 21-27). A study entitled “the effectiveness of interventional program in executive function in MS” confirmed the effectiveness of this program in improving executive functions and verbal learning in MS patients in the experimental group compared to the controls. The effects of this intervention on verbal learning remained unchanged after one year (21).

A single-case (AB model) experimental study conducted by Khalili et al. investigated the effect of attention rehabilitation on reducing focal attention deficits and working memory in six MS patients based on Sohlberg and Mateer’s attention assignments (attention process training, APT) and using the Wechsler adult intelligence scale (WAIS), the digit span of the Wechsler memory scale (WMS), multiple sclerosis neuropsychology questionnaire and the Beck’s depression inventory. These authors concluded that attention rehabilitation reduces the deficits of focal attention and working memory in MS patients (28). A study by Ghamarigivi et al., entitled “Investigation of cognitive rehabilitation on reconstruction of executive functions of obsessive-compulsive patients”, showed that cognitive rehabilitation is effective in the reconstruction of executive functions in these patients (24).

Brain imaging studies have shown that teaching cognitive functions and basic skills can change the amount of the gray matter and synaptic activity (29). A neuron losing inputs from damaged neurons can form new dendrites or strands to receive information from another neuron in the same current or a neuron in a further current. MS studies on imaging neuron plasticity processes following cognitive or motor therapies found patients with low or moderate performance in cognitive or motor assignment to show enhanced performance in aligned and non-aligned regions while performing the tasks (30). Moreover, based on the principle of plasticity and self-restoration of the brain, computer-assisted cognitive rehabilitation creates stable synaptic changes in less active regions of the brain through successive stimulations (31). Hardy et al. investigated the effectiveness of the Captain’s Log cognitive rehabilitation program in improving active memory and attention. This program comprised twelve 50-minutes sessions, once a week, and confirmed the effectiveness of the program and its applicability in improving the patients’ cognitive functions in the intervention group, consisting of cancer-treated adolescents (32).

According to the human brain plasticity hypothesis, in case less active regions are properly and repeatedly stimulated, such changes cannot be temporary, and will remain stable owing to the changes they create in the structure of

neurons (33). Improving cognitive functions involved in MS can therefore help improve cognitive problems in MS patients and treat them and improve their quality of life. Using computer-assisted cognitive rehabilitation can be effective as a new method.

### 5.1. Conclusions

According to the results obtained, computer-assisted rehabilitation can improve executive functions in MS patients. The significant results associated with the components of executive functions, i.e. cognitive flexibility and inhibitory control; also confirm the effectiveness of cognitive rehabilitation in improving the efficacy of these components.

The present study limitations included failing to follow-up the patients due to the unavailability of the patients participating in the rehabilitation sessions. In addition, the sample size could not be increased to generalize the findings.

Given the present results confirming the effectiveness of cognitive rehabilitation in executive functions, this program is recommended to be used in conjunction with medicinal therapies and motor rehabilitation in MS patients. This method is recommended to be used in specialized and rehabilitation clinics for other disorders, including dementia, Alzheimer’s and Parkinson. This program can also be used in generally healthy individuals to help improve their quality of life and increase their occupational productivity.

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### Footnotes

**Conflict of Interests:** It is not declared by the author.

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