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The Possibilities and Limits of the Rehabilitation of Cognitive Functions in Patients with Multiple Sclerosis Using a Computer Program

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Abstract

Objectives: The purpose of the current study was to evaluate whether a 12-week neuropsychological rehabilitation program has a positive effect on the improvement of cognitive functions and what methods can be used to measure this effect. Furthermore, this study intended to verify the effect of the chosen training plan on the resulting state of cognitive functions, in particular with regard to the frequency and duration of the plan.

Methodology: Fifty-eight patients diagnosed with MS were randomized into an experimental condition or the control group, 15 patients were excluded from the study. The experimental condition included 26 patients (22 women and 4 men), whole the control group consisted of 17 patients (12 women and 5 men). All of these patients had a cognitive defect that was assessed at the beginning of the study and monitored using the neuropsychological tests after the participation in the training program. Participants in the experimental group received their rehabilitation of cognitive functions using a PC training program, which they completed in their home environments (30 mins/4 times per week, for 8 consecutive weeks). Overall, there were 32 training sessions on predetermined days with a specific detailed training plan. The control group received no training. The neuropsychological tests used at the beginning and the conclusion of the study showed a positive effect of the training program, while the greatest improvement was seen in the areas of immediate memory and attention.

Results: The results showed a positive effect related to neuropsychological rehabilitation in MS patients that received regular training four times per week for eight consecutive weeks.

Keywords: Multiple Sclerosis (MS); Neuropsychological rehabilitation; Attention; Memory; Computer cognitive training

Introduction

Multiple sclerosis (MS) is one of the most common neurological diseases and at the same time one of the most common causes of chronic neurological disability in young adults. MS leads to motor as well as cognitive and neuropsychiatric symptoms. Cognitive disorders can occur independently of physical disability, which can complicate their recognition or assessment. Cognitive deficits are most often characterized by mild cognitive impairment and in the more advanced stages by subcortical dementia. The deficit is commonly observed in complex attention, the efficiency of information processing, executive functions, processing speed (information) and long-term memory [1]. Cognitive changes can occur at any time during the illness and sometimes as the primary symptom. Generally, it can be said that two patients with this disease do not have exactly the same symptom profile or disease progression [2]. Cognitive disorders are very common, but they are hardly noticeable at first, which is the reason why they tend to escape the attention of everyone for years [3]. According to the neurological studies, cognitive function (CF) deteriorate in 50-75% of patients [4]. In the last decade, diagnostic criteria and medications have been improved to modify the disease, which in turn leads to early diagnosis and treatment. Furthermore, good cognitive training can minimize the impact of the illness on the quality of patient´s life. However, the methods of such training are not unequivocally methodically or therapeutically fixed at this time. For this reason, studies in the last decade have been trying to address the question of whether there is an effective rehabilitation strategy, which could lead to the compensation of damaged brain structures and restoration of cognitive functions, due to the plasticity of the brain and the ability to restructure neural networks [5]. In the past, training was focused predominantly on learning and memory functions. Nevertheless, attention is now being transferred to the training of executive functions and attention [6]. At the same time, there have already been studies confirming that restructuring of the neural networks within the CNS is possible under the influence and in response to external stimuli, environmental changes or injuries [7]. Nonetheless, there are only few studies that investigated the mechanisms of targeted rehabilitation more precisely. Likewise, studies that are available provide only fragmented or incomplete data [8]. In 2013, A. Mantynen et al. [9] published a randomized controlled trial that involved 102 patients with relapsing remitting MS. The authors concluded that neuropsychological rehabilitation did not improve cognitive performance, but reduced the perception of patient´s cognitive deficit and thereby positively influenced their quality of life. What this means is that although the effect has not been clearly demonstrated in the test techniques, patients were subjectively feeling better. The results of this study showed that the direction of focusing on the emergence of randomized controlled trials with a sufficient number of patients that occurred post 2008 is commendable, nevertheless, it is clear that even the results of these studies may not be relevant to the assessment of the effect of rehabilitation of cognitive functions. More specifically, these studies showed that a precisely targeted training is necessary for a demonstrable positive effect (in comparison to any

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kind of training) and that what we consider to be very important is the necessity of correct time distribution and sufficient frequency of repetition. Two studies in the years 2014-2015 were published that provided a systematic overview of the experience of cognitive function training in patient with MS. The first was a meta-analysis assessing the effects of cognitive intervention in MS including only RCTs with comparable conditions [10], while the second was a study focused on the identified conflicting findings in the published literature about the effectiveness of various forms of cognitive rehabilitation techniques used in patients with MS [6]. Both studies agreed that the training of cognitive functions has a positive effect on patients and that this training should be an integral part of comprehensive care for patients with MS. Nevertheless, these studies also point to the contradictory results of previous research, in terms of used measurement techniques, training methods and training plans. Some of the frequent methodological problems include the small sample size, the absence of a control group and the problems related to output measurements. The insufficient quality of output measurement may be the reason why we do not record all the possible changes and thus, do not capture the possible positive effect [6]. A systematic review published in 2015 discussed old and new studies, described the current state of this field and provided direction for an ongoing MS research. Authors concluded that training of psychiatric activities causes improvement in cognition and brain function; however, it is not clear to what extent the brain is capable of plasticity. This research identified contradictory results related to the efficacy of various rehabilitation techniques and therefore, no definitive conclusions can be drawn on the effect of cognition, mood, quality of life, fatigue or how patients perceive this effect. Another explanation may also be related to the selection of the output measures that were used in these studies and that may not be reliable to ascertain all the possible effects. If output measures are not able to detect the changes, it does not mean that the examined rehabilitation exercise is not effective, but rather that an insufficiently sensitive output measure has been used instead – i.e. a possible positive effect has not been detected, which likely led to incorrect conclusions [6].

All of the above mentioned facts have lead the research team of the psychiatric clinic to try create and implement a rehabilitation procedure without the known negative factors and find an evidence-based rehabilitation process. We have therefore attempted to create a recommended set of procedures related to the rehabilitation of cognitive function in patients with MS, which are based on the conclusions of the studies discussed in this article and at the same time tried to investigate this procedure in a form of a randomized study with a control group.

Materials and Methods

Patients

The following inclusion criteria were used: a diagnosis of Multiple Sclerosis, the score of 0-6 on the Expanded Disability Status Scale (EDSS), age 18-65, functional dominant upper limb (in order to handle the work on computer) and an access to a computer with an Internet connection in the training environment. Patients with a history of drug or alcohol abuse, major psychiatric disorder, acute relapses, neurological disease other than MS or patient with an ongoing rehabilitation were excluded. In order to verify the information obtained from the patients regarding their past medical history, hospital records were examined as necessary. All patients provided their written informed consent and the study protocol was approved by the ethics committee of the Charles University Medical Faculty in Pilsen.

Eighty patients were suggested to participate in this study, however, 22 patients did not meet the inclusion criteria. Fifty-eight patients were randomized to the experimental a control groups. Thirty-five patients were assigned to the experimental group and 6 patients from this group were excluded due to the lack of training conditions and 3 due to the health reasons. Statistical analyses included 26 patients (22 females and 4 males) in the experimental group. Twenty-three patients were randomized to the control group and 6 patients were excluded due to the health reasons. Statistical analyses included 17 patients (12 females and 5 males). The reason for exclusion was any health problem with duration more than three days or change of medication during the study.

There were no significant differences in age (experimental group had an average age of 41.3 years, SD=6.5, control group had an average age of 42.4 years, SD=9.2, Mann-Whitney U test, U=231, Z=0.19 (Pearson Chi-square: 1.22, df=1, p=0.27), in education (Pearson Chi-square: 1.30, df=3, p=0.73), in the level of disability (Pearson Chi-square: 2.3, df=3, p=0.51) or in the EDDS score (the experimental group had an average score of 3.1, SD=1.4, while the control group had an average score of 3.3, SD=2.0; U=218.5, Z=-0.06, p=0.95).

Interventions and outcome assessment

The assessment battery was designed to target trained functions, while at the same time, it was sensitive enough to record any changes in patients with mild cognitive defects. The battery included carefully chosen testing techniques and self-assessment questionnaires that were selected based on the results from previous studies, where positive results were found either only in the testing methods and not in the subjective evaluation [11] or purely in the subjective evaluation of the patients [12]. Furthermore, we also included techniques related to the possible changes in the field of emotions.

The neuropsychological testing

1. Repeatable Battery for the Assessment of Neuropsychological Status (R-BANS), Christopher Randolph. The Repeatable Battery for the Assessment of Neuropsychological Status (R-BANS), is a brief, individually administered test, which measures attention, language, Visuospatial/Constructional abilities and immediate and delayed memory. The test comprises 12 subtests that can be administered by trained examiners in about 20 to 30 min. R-BANS are intended for use with adolescents and adults, ages 12 to 89 years. Normative scores were developer using a stratified, nationally representative sample of 69 healthy adolescents and adults.

2. Trail Making Test (TMT), The Trail Making Test is a neuropsychological test of visual attention and task switching. It consists of two parts, in which the subject is instructed to connect a set of 25 dots as quickly as possible while still maintaining accuracy. The test can provide information about visual search speed, scanning, speed of processing, mental flexibility, as well as executive functioning. It can sensitively detect cognitive impairment. This test was a part of the Halstead-Reitan Neuropsychological Battery.

The self-assessment questionnaires and measures

1. The Cognitive Failures Questionnaire CFQ [13] is a self-assessment questionnaire that focuses on the examination of cognitive function disorder in routine daily activities.

2. A range of somatic well-being and A range of psychological well-being are self-assessment measures related to the current psychological and somatic well-being. These are 10-point Likert type scales ranging from 0-10.

3. The Schwartz SOS 10 scale is a 10-item scale intended for the field of psychiatry and psychology with regard to the evaluation of therapy. The purpose of this measure is to assess the effectiveness of treatment across a wide range of treatment facilities and various populations. This measure has been shown to have good psychometric properties [14].
4. Beck Depression Inventory-II is a psychodiagnostic questionnaire assessing the presence and severity of depression. This questionnaire is frequently used in the field of clinical psychology and neuropsychology as a screening measure of the actual severity of depression.
5. Hamilton's scale of depression (HAMD) [15].

The neuropsychological rehabilitation

All patients participated in an entry examination that consisted of a neuropsychological battery. Subsequently, patients in the experimental group received training on the Happy Neuron Brain Jogging computer program, which they were later asked to work on from their homes.

The program contains 20 different task and trainings related to memory, concentration, speech, logical thinking, special orientation and other abilities. Different levels of difficulty can be adjusted, thereby achieving high variability in exercise. This program also includes and "an automatic coach", who is able to select the necessary set of exercises, in order for the patient to improve. Therefore, this program can also be used by patients that are currently unable to train under the direction of a clinical psychologist or a neuropsychologist.

The training plan was designed for four times per week/30 mins per session for eight consecutive weeks. Overall, there were 32 training sessions on predetermined days with a specific training plan.

The primary goals of training included the following cognitive functions:

- Memory
- Attention and concentration
- Speed and information processing
- Executive functions
- Expression and speech comprehension
- Spatial orientation and perception

The training was primarily focused on the enhancement of attention concentration, memory stimulation, improvement of logical thinking and the expansion of vocabulary. Likewise, the primary goal was to achieve improvements in the area of attention concentration, immediate memory, speech, delayed recognition and visual-spatial perception.

All patients obtained a training sheet, which included two exercises that were same for all participants, with the requirement to repeat the exercise exactly three times. For the remaining time (total training time was 30 mins), participants were asked to choose an exercise at their discretion. For example, if the participant completed the required exercise in 25 mins, he or she could choose another exercise at their discretion for the remaining five minutes. The patient also received a written training instruction that it is better to repeat one exercise multiple times rather than doing more exercises only once. Patients were required to fulfill all 32 training blocks. The results for each training session were recorded immediately after the session was completed on a designated website. If and when needed, communication with patients was also carried out through this website. Other communication was conducted through email and phone conversations. For example, if the administrator noticed that the training had not been completed, he contacted the patient to find out the reason and to figure out how to continue the training.

The control group received no training. In order to control for placebo effect, the control group was repeatedly contacted for a period of two months (three times in total) and asked to report their current psychological status by completing a prepared questionnaire. The recorded and quantified improvement of the control group was deducted from the results of the experimental group.

In the last phase of the trial, all patients from the experimental and control group completed a final neuropsychological battery testing.

Results

Statistical analyses

Results of the neuropsychological batteries: The experimental group participated in a computer rehabilitation program of cognitive functions in the duration of eight consecutive weeks at home (four times per week/30 mins per session). There were overall 32 training sessions that took place on predetermined days with a specific training plan. The control group received no training and kept only minimal contact with the therapeutic team. Patients in the control group were contacted exactly three times and asked to complete a questionnaire about their current mental health state.

After eight weeks of initial testing, both the experimental and control groups were screened by neuropsychological batteries with the following results.

Initial examination has shown that the experimental and control groups did not significantly differ in the total score or in any of the five given RBAN-S sub-groups prior to the initial training. However, following the training, the experimental group received higher scores in all given variables and obtained significantly higher total score (Mann-Whitney U test, $z=2.411$, $p<0.05$) and significantly higher scores on Immediate memory (U test, $z=1.982$, $p<0.05$), Attention ($z=2.444$, $p<0.05$) and Delayed recognition ($z=2.277$, $p<0.05$).

Thus, the experimental group showed statistically significant improvements in the total RBAN-S score and in some of the RBAN-S sub-groups, except for "Speech" (Table 1), whole the control group showed statistically significant improvements for "Short-term memory" ($p<0.05$). No other significant changes were observed within the control group.

The experimental group improved in all RBAN-S variables with a minimum of 5.8 points (5.7% increases) in the "Language" domain and up to 13.6 points (14.5% increase) in the total score. The control group showed even some deterioration in some of the variables, where the smallest change was -5.7 points (-5.5% drop) in the "Immediate memory" domain to a maximum improvement of 5.3 points (5.9% increase) in the total score. An essential part of the project was also the exclusion of "practice effect" from the results of the study. This exclusion was achieved by the comparison of the results between the control and experimental groups, where the work with control and experimental groups was the same, except for the targeted cognitive training that was fulfilled only for the experimental group. If we considered the total score for the control group as a "practice effect" (with no intervention in the sense of a targeted cognitive training) and deducted this effect (5.3

	Experimental group (N=26)		Control group (N=17)	
	Z	p-hodn.	Z	p-hodn.
RBANS1 Total ý & RBANS 2 Total	4.903	p<0.001	-0.25	ns.
percentile & percentile	4.903	p<0.001	0.25	ns.
Immediate Memory & Immediate Memory	2.502	p<0.05	2.25	p<0.05
Visuospatial/Constructional & Visuospatial/Constructional	2.919	p<0.01	1.206	ns.
Language & Language	1.668	ns.	0.516	ns.
Attention & Attention	3.47	p<0.001	0.516	ns.
Delayed Memory & Delayed Memory	3.878	p<0.001	0.97	ns.

Table 1: Results including the "practice effect".

points), the experimental group would still show statistically significant net effect of the intervention by 8.3 points.

Mann-Whitney U test shows statistical probativeness of a given indicator– "ns." for non-significant.

Table 1 clearly shows statistically verifiable positive effect related to the cognitive function training.

The Figure 1 clearly shows better results for the experimental group.

The TMT neuropsychological test was used in the study with the following results. The comparison of both groups (the experimental and control groups) showed no significant differences. The comparison of the results for both groups in terms of the intake and exit examinations is shown in Table 2.

The TMT test results showed significant improvement in attention concentration, even after the "practice effect," measured within the control group, was taken into account.

Results of the self-report measures and other cognitive tests: No statistically significant differences for the experimental and control groups were observed for all utilized methods prior to the training. Likewise, no statistically significant differences were recorded after the training.

The evaluation of the results for these techniques is shown in Table 3.

The data comparison of the self-assessment measures gathered during the input and exit interviews was demonstrably better in favor of the experimental group. An improvement was seen across all five scales, while the improvement in the most objective BDI scale was statistically significant on average 4.6 points. Nonetheless, some improvement was also seen in the control group and when standard deviation was included in the comparison, no statistically significant improvement was observed for the experimental group. Thus, the improvement in subjective perception can occur without targeted cognitive training, in particular if the patient feels that enough time is being devoted to him or her. As for the objective indicators, however, this improvement is not visible.

The overall evaluation

In terms of the assessment of results, subjective and objective techniques and measures have to be evaluated separately. Statistically significant improvements for the experimental group were observed in nearly all objective tests (Table 4).

As for the self-assessment scales, the results are less pronounced (Table 5).

The comparison of the objective and self-assessment measures clearly showed that the objective techniques demonstrated a significant positive effect related to the cognitive training conducted within this

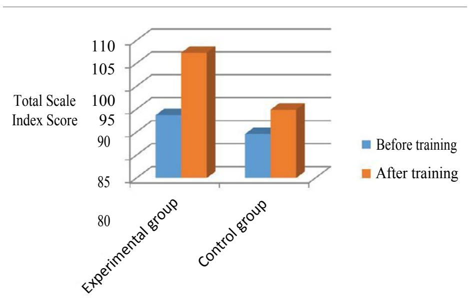

Figure 1: The overall results for the control and experimental groups are shown in following picture. The picture clearly shows better results for the experimental group.

	Experimental group (N=26)		Control group (N=17)	
	Z	p-hodn.	Z	p-hodn.
TMT A & TMT A	2.157	p<0.05	1,455	ns.
TMT B & TMT B	2.8	p<0.01	0	ns.

Table 2: Comparison of TMT test results.

	Experimental group (N=26)		Control group (N=17)	
	Z	p-hodn.	Z	p-hodn.
BDI & BDI	3.062	p<0.01	-0.267	ns.
HAMD & HAMD	3.801	p<0.001	0.289	ns.
CFQ & CFQ	0.4	ns.	0.75	ns.
SOS & SOS	2.245	p<0.05	0.485	ns.
SP & SP	0.417	ns.	0.289	ns.
PP & PP	1.376	ns.	1.664	ns.

Table 3: The results of the self-assessment questionnaires for the experimental and control groups.

	Experimental group (N=26)		Control group (N=17)	
	Z	p-hodn.	Z	p-hodn.
RBANS & RBANS	4.903	p<0.001	-0.25	ns.
TMT A & TMT A	2.157	p<0.05	1.455	ns.
TMT B & TMT B	2.8	p<0.01	0	ns.
HAMD & HAMD	3.801	p<0.001	0.289	ns.

Table 4: The results of the objective measures for the experimental and control groups.

	Experimental group (N=26)		Control group (N=17)	
	Z	p-hodn.	Z	p-hodn.
BDI & BDI	3.062	p<0.01	-0.267	ns.
CFQ & CFQ	0.4	ns.	0.75	ns.
SOS & SOS	2.245	p<0.05	0.485	ns.
SP & SP	0.417	ns.	0.289	ns.
PP & PP	1.376	ns.	1.664	ns.

Table 5: The results of the subjective measures for the experimental and control groups.

study. If only self-assessment measures were to be used, the positive effect of such training could not be clearly demonstrated.

As for the most efficient RBANS test battery, a significant improvement has been observed in the immediate memory sub-scores and in the "Visuospatial/Constructional". On the other hand, the lowest score was found in the "Language" sub-score. The results of this study do not clearly explain the difference in effect of the cognitive training preformed for the various categories of cognitive functions. We assume that a significant influence lies within the fact that the proposed cognitive exercises almost always contain a memory component – i.e. even exercises related to speech function train this memory component while also training attention.

Discussion

Relatively few studies have been conducted until 2008 that focused on the treatment of cognitive disorders. Although some studies revealed the benefits of cognitive rehabilitation for people with MS, others have shown no improvement. The conclusions of these studies were, however, limited by methodological problems, such as initial differences between groups, the use of qualitative rather than quantitative research and the need to rely on case studies. This prompted the need for methodologically thorough research ideally with a placebo-controlled, randomized design [2]. In 2013, Mantynen et al. [9] published a randomized controlled trial involving 102 patients with relapsing reminiscent MS. Patients were randomly assigned into two groups, training and control groups. The training group received rehabilitation for cognitive function once a week in 60 min sessions for 13 weeks. The control group received no training. Neurological intake and exit interviews were conducted for both groups. The authors concluded that neuropsychological rehabilitation did not improve cognitive performance, but reduced the perception of patient's cognitive deficits and thereby positively influenced their quality of life. This means that although the effect has not been clearly demonstrated in the used testing material, patients reported to subjectively feel better. Other studies have shown the importance of taking into account that plasticity represents the basic developmental ability of the brain, learning and memory even for healthy individuals. In the context of MS, this term encompasses molecular, synaptic and cellular events and even the reorganization of the cortex or fibers that lead from acute or chronic damage to recovery. A very promising method for evaluating this theory is magnetic resonance imaging (MRI), functional magnetic resonance imagining (fMRI) and DTI imaging [16]. The use of these advanced MRI techniques has recently demonstrated that plasticity and functionally relevant long-term reorganization processes are preserved in most advanced stages of the disease and that these phenomena are functionally important to maintain motor and cognitive functions. Nonetheless, only few studies explored the mechanism of the targeted rehabilitation up to this point. Another deficiency lies in the fragmented and incomplete data provided in the available studies, despite of the fact that cognitive and motor rehabilitation play a key role in the care of the patients with MS [8].

The purpose of our study was therefore to build upon the aforementioned need for objective research, while trying to suppress the all known effects from previous studies that lead to unproductive results. Therefore, the initial requirement was to produce a study with a number of patients that allowed for a discernible statistical evaluation, while at the same time allowing for a wide range of testing techniques to be used. The cited studies always included either a low number of patients, which allowed for very unproductive quantitative evaluation [17] or the studies that allowed for large number of patients utilized only a limited amount of testing material, which influenced their conclusions – the use of only self-assessment methods does not show the objective condition of the patient, but only reflects on his/her own assessment of the situation, which can be influenced for example only by the fact that someone is interested in the patient [4]. Thus, by combining the needs for statistical evaluation and the possibility of using a wide range of testing material, we have addressed these shortcomings and intended to enroll approximately 20-30 patients for both groups.

Among other factors, the frequency and duration of training sessions have been shown to have a major impact on the effectiveness of the training. For example, training only once per week lead to improvements only for some of the features. Likewise, study by Tesar et al. [18] showed significant improvements in executive function and special-constructional abilities, but no significant improvements in memory or fatigue values. Furthermore, Mantynen et al. [12] showed a positive effect of the rehabilitation of cognitive functions on perceived cognitive impairment. Decreased levels of depression and fatigue were also noted. However, these results were verified only with the use of self-assessment scales. On the other hand, training the occur 3-6 times per week for 6-12 weeks showed improvement that was manifested in a number of cognitive functions [19,20]. Some patients even experienced improvements in activities of daily living [21] and improvements in emotion [19,22,23]. After the examination of a systematic review [6,10] we have chosen a training four time per week with 30 minutes per session for eight consecutive weeks. Therefore, we had 32 training sessions overall that took place on predetermined days and included a specific training plan. The duration of the training was carefully chosen to allow for the notation of positive and verifiable results. Some of the previous studies used short or low intensity training – e.g. no improvement in cognitive performance, but a positive effect on cognitive deficit was found [9]. We believe that training once a week for 60 mins cannot lead to objectively measurable improvement, but that only the subjective perception of patients may be positively influenced by such training. Based on the comparison and examination of individual studies, we decided the target training time of approximately four times per week for at least two months.

Patients perceived this training very positively. The use of the Happy Neuron Brain Jogging software has proven to be very useful in fine tuning the patients and for the adherence to the training parameters outside of the sessions with the therapist. Patients viewed the software as user-friendly. They received the instruction to perceive this training as an entertainment rather than rehabilitation and as an opportunity to actively participate in the improvement of their condition. This recommendation has been accepted without any difficulty.

The training results were recorded immediately after the end of the training session with the help of a specifically devoted web program. In the event of a breakdown in the prescribed training program, the patient was contacted. This ensured a strict adherence to the prescribed training conditions.

A great deal of attention was paid to the assembly of test battery. We intended to compile a battery focused on trained functions, while trying to be sensitive enough to changes in patients with mild cognitive deficit. Based on the review of previous studies [11,12], the testing methods included objective as well as self-assessment measures. We also included methods that focused on the changes in the area of emotions. The objective part of this research examined the quantitative indicators, while the subjective part of this research allowed eliminating the placebo effect that was measured in the control group. Furthermore, this shows the importance of using the control group – since most of the published studies include a control group, but do not always control for the placebo effect and the results of the experimental and control groups generally do not differ [24]. Therefore, we included a wide range of testing methods – both objective (RBANS, TMT, etc.) and subjective (BDI-II, HAMD, SOS, SP/PP, CFQ).

An important part in the evaluation of the results was to eliminate the practice effect, which occurs in both the experimental and control condition and which is also measurable by objective test methods. The reduction of the practice effect measured in the control group from the results of the experimental group will show the actual effect of the measured cognitive training.

Patients did not participate in any other form of cognitive training and did not use cognitive enhancing drugs during this study.

Our study presented statistically significant improvements for patients included in the experimental group, while no change has been seen in patients in the control group, after controlling for the practice and the placebo effects. As for the RBANS battery, the results of the experimental group showed the greatest improvement in the immediate memory and Visuospatial/Constructional coordination, which corresponded with the used Neuron software technology that focused on graphic objects rather than purely verbal objects.

The results of this study demonstrate the positive effect of a neuropsychological rehabilitation in patients with MS that participate in a regular training four times per week for eight consecutive weeks.

Limitations

The efforts to control for placebo effect and the practice effect recommend to use three groups of patients – an experimental group, a placebo group that would be kept in some contact with the research team and a control group that would have no contact with the research team, in order to obtain a more accurate assessment of the training results. In our study, the control group would ideally play the role of the placebo group. Nevertheless, the comparison of the results between the placebo and control groups would allow for a targeted elimination of the placebo effect from the practice effect. We perceive the practice effect as the effect that arises during testing and that is manifested in both the experimental and control groups and as such should be eliminated.

However, this influence of a practice effect should be differentiated from the above mentioned placebo effect.

This study also did not include follow-up examinations. These would be useful for demonstrating (or disproving) the sustained effect of the measured improvement in patient´s cognition.

Conclusion

The results of this study show a positive effect of a neuropsychological rehabilitation in patients with MS in the above mentioned and clearly structured training. Furthermore, the results showed improvements for the experimental group in the overall RBANS testing battery and in other objective techniques. The improvements were shown to be statistically significant – even after accounting for the practice effect measured in the control group. The greatest improvement occurred in the areas of memory and attention.

In conclusion, a rehabilitation of cognitive function has a positive effect in patients with MS, provided that certain set of criteria are met, both within the diagnostic process and especially within the training program. The essential part lies not only in the sufficient frequency of the training, but also in its distribution over time. The training in our study occurred four times per week with 30 mins sessions/time. A shorter time for training seems to be ineffective, while longer training times lead to increased fatigue and memory concentration problems in patients with MS. Another important training factor was the used software. In this case, Happy Neuron Brain Jogging was used and patients rated this software as user-friendly and interesting. From our point of view, the program fulfilled the requirements for training of certain functions that our study was targeting. The patients received and kept this training in a form of a CD, while they could continue their training after the termination of the project. A suggestion for further research is certainly the long-term effect of such training.

We assume that the positive effect of the rehabilitation program can have a significant impact on improving the quality of life of MS patients and improve their chanced at obtaining an employment. This, however, also needs to be confirmed by studies focused on the quality of life of MS patient.

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