

RehaCom<sup>®</sup>

# EFFECTIVENESS- STUDIES



HASOMED<sup>+</sup> Certified Medical Devices



## Proven track record

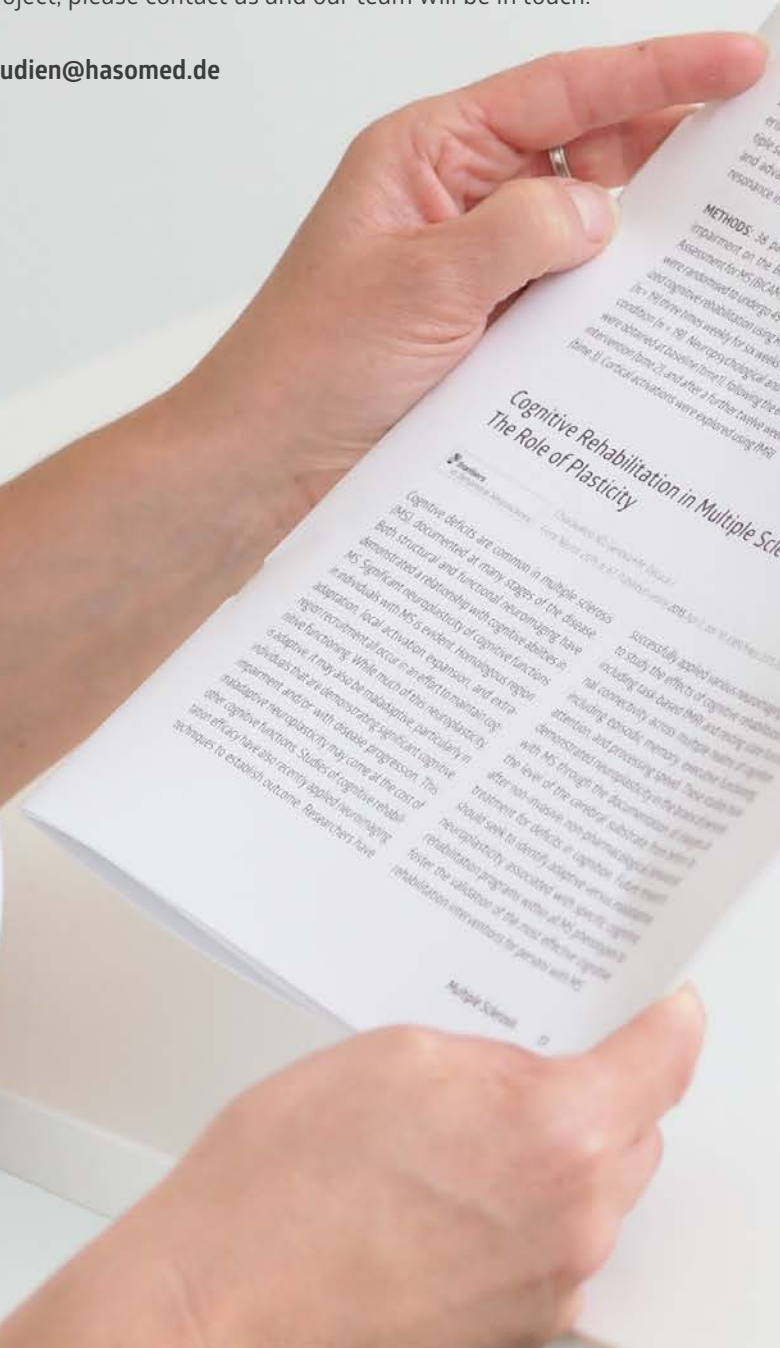
RehaCom has an outstanding record for almost 30 years of strong and sustainable results in clinical settings. Numerous studies utilized RehaCom and demonstrated the efficacy and feasibility. All listed studies were carried out with RehaCom.

## Would you like to conduct a study with RehaCom?

To support the growing body of research studying the efficacy of cognitive training, RehaCom's scientific team partners with research institutions all around the world to study how RehaCom helps with a variety of neurological and psychiatric conditions.

If you are interested in using RehaCom in your research project, please contact us and our team will be in touch.

[studien@hasomed.de](mailto:studien@hasomed.de)



# Studies and Systematic Reviews

## ACQUIRED BRAIN INJURY

from Page

Traumatic brain injuries (TBI) / Stroke (CVA)	17 studies	2001-2020	4
Cognitive disorders following chemotherapy	1 study	2020	13

## NEURODEGENERATIVE DISEASES

Multiple sclerosis (RRMS/SPMS)	21 studies	1998-2020	14
Parkinson's Disease	2 studies	2014-2015	27
Mild Cognitive Impairment (MCI)	1 study	2019	29
Dementia / Alzheimer's Disease	3 studies	2003-2018	30

## PREVENTION OF COGNITIVE DETERIORATION / GERIATRICS

Healthy Aging	2 studies	2006-2018	32
Cognition and balance abilities of the elderly	1 study	2013	33

## NEURODEVELOPMENTAL DISORDERS

Attention-deficit hyperactivity disorder (ADHD)	1 study	2013	34
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## MENTAL ILLNESS

Schizophrenia	9 studies	2006-2019	35
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## COMBINATION THERAPY

RehaCom and rTMS (Alzheimer's disease)	1 study	2020	42
RehaCom and tDCS (Stroke/CVA)	1 study	2018	43
RehaCom and VR (Stroke/CVA)	1 study	2019	44
RehaCom and Tai Chi (TBI)	1 study	2020	45
RehaCom and Acupuncture (Stroke/CVA)	1 study	2016	46

### Efficacy of RehaCom cognitive rehabilitation software in activities of daily living, attention and response control in chronic stroke patients.



Veisi-Pirkoochi, S., Hassani-Abharian, P., Kazemi, R., Vaseghi, S., Zarrindast, M. R., & Nasehi, M. (2020). Journal of Clinical Neuroscience, 71, 101-107.

**BACKGROUND:** Our world is unfortunately facing a huge number of stroke. Attention, response control and activities of daily living (ADL) are important cognitive functions affected by stroke. In line with this explanation, we aimed to investigate the effect of RehaCom rehabilitation software on ADL, attention and response control in chronic stroke patients with damage to middle and anterior cerebral arteries.

**METHOD:** For selecting participants, among chronic stroke patients who referred to our special rehabilitation clinic for patients with stroke, fifty patients selected. Participants were assigned to control (n = 25) and experimental (n = 25) groups. The experimental group was compared with the control group before and after using RehaCom (ten 45-min sessions in five weeks).

**RESULTS:** There is a significant enhancement in ADL, attention and response control scores in the experimental group compared with the control group. In fact, treatment with RehaCom significantly improved the score of all studied variables in chronic stroke patients.

**CONCLUSIONS:** In conclusion, RehaCom cognitive rehabilitation software has improvement effect on ADL, attention and response control in patients with chronic stroke. Our study reveals a new information about the efficacy of computerized training in the rehabilitation of stroke patients.

### The effect of high vs. low intensity neuropsychological treatment on working memory in patients with acquired brain injury.



Weicker, J., Hudl, N., Hildebrandt, H., Obrig, H., Schwarzer, M., Villringer, A., & Thöne-Otto, A. (2020). Brain Injury, 1-10.

**METHODS:** All patient underwent 4 weeks of compensation therapy in a day-care setting. In addition, they received either 20 sessions of computer-based WM training (n = 11) or attention training (n = 9). Transfer effects on cognition and their functional relevance in daily life were assessed before treatment, after 2 weeks (10 additional training sessions), and after 4 weeks (20 additional training sessions) of therapy.

**RESULTS:** The combined treatment led to significant improvements in WM performance, verbal memory, and self-reported changes in daily life. The amount of

training was identified to modulate efficacy: Significant improvements showed only in the later training phase. We observed no differences between the two training schemes (WM vs. attentional training).

**CONCLUSIONS:** Even in the chronic phase after brain lesion WM performance can be enhanced by the combination of compensation therapy and computerized cognitive training when applied intensely; both a more general attention and a specific WM training regimen are effective.

# Evidence-Based Cognitive Rehabilitation: Systematic Review of the Literature From 2009 Through 2014

Archives of Physical Medicine and Rehabilitation

Cicerone KD, Goldin Y, Ganci K, Rosenbaum A, Wethe JV, Langenbahn DM, Malec JF, Bergquist TF, Kingsley K, Nagele D, Trexler L, Fraas M, Bogdanova Y, Harley JP. Arch Phys Med Rehabil. 2019 Aug;100(8):1515-1533. doi: 10.1016/j.apmr.2019.02.011.

**Objectives:** To conduct an updated, systematic review of the clinical literature, classify studies based on the strength of research design, and derive consensus, evidence-based clinical recommendations for cognitive rehabilitation of people with traumatic brain injury (TBI) or stroke.

**Data Sources:** Online PubMed and print journal searches identified citations for 250 articles published from 2009 through 2014.

**Study Selection:** Selected for inclusion were 186 articles after initial screening. Fifty articles were initially excluded (24 focusing on patients without neurologic diagnoses, pediatric patients, or other patients with neurologic diagnoses, 10 noncognitive interventions, 13 descriptive protocols or studies, 3 nontreatment studies). Fifteen articles were excluded after complete review (1 other neurologic diagnosis, 2 nontreatment studies, 1 qualitative study, 4 descriptive articles, 7 secondary analyses). 121 studies were fully reviewed.

**Data Extraction:** Articles were reviewed by the Cognitive Rehabilitation Task Force (CRTF) members according to specific criteria for study design and quality, and classified as providing class I, class II, or class III evidence. Articles were assigned to 1 of 6 possible categories (based on interventions for attention, vision and neglect, language and communication skills, memory, executive function, or comprehensive-integrated interventions).

**Data Synthesis:** Of 121 studies, 41 were rated as class I, 3 as class Ia, 14 as class II, and 63 as class III. Recommendations were derived by CRTF consensus from the relative strengths of the evidence, based on the decision rules applied in prior reviews.

**Conclusions:** CRTF has now evaluated 491 articles (109 class I or Ia, 68 class II, and 314 class III) and makes 29 recommendations for evidence-based practice of cognitive rehabilitation (9 Practice Standards, 9 Practice Guidelines, 11 Practice Options). Evidence supports Practice Standards for (1) attention deficits after TBI or stroke; (2) visual scanning for neglect after right-hemisphere stroke; (3) compensatory strategies for mild memory deficits; (4) language deficits after left-hemisphere stroke; (5) social-communication deficits after TBI; (6)metacognitive strategy training for deficits in executive functioning; and (7) comprehensive-holistic neuropsychological rehabilitation to reduce cognitive and functional disability after TBI or stroke.

**EFFICACY OF REHACOM SPECIFICALLY:** RehaCom specifically has been studied as well. Two of the most encouraging and rigorous studies utilizing RehaCom demonstrated specific effectiveness in memory and in executive functioning. The studies found increased connectivity in cerebral functional connectivity of the hippocampus with frontal and parietal cortical areas and improvements in attention and new learning. Additionally, working memory training resulted in significant improvements on working memory, word fluency and prospective memory performance. Both, a direct benefit and a generalization of training effects have been indicated.

# Comprehensive cognitive training improves attention and memory in patients with severe or moderate traumatic brain injury



Leśniak MM, Iwański S, Szutkowska-Hoser J, Seniów J

Applied Neuropsychology 2019 Mar: Adult, DOI: 10.1080/23279095.2019.1576691

Traumatic brain injury (TBI) leads to cognitive disorders, the most frequently affected functions being attention and memory. The present study aimed to investigate the effects of a cognitive rehabilitation program, consisting of individual and group interventions, on attention and memory in patients with TBI. Fifteen patients—in the postacute phase of recovery from moderate-to-severe TBI and subsequent cognitive disorders—were enrolled on a three-week waiting list and then underwent a three-week cognitive rehabilitation program. The patients were assessed using a set of five neuropsychological attention and memory tests. The patients and their caregivers were questioned to assess subjective

changes in the everyday functioning of the former. The introduction of cognitive training was associated with improvement in one memory test and in two measures of attention. Mean effect size across all tests was higher over the period with treatment compared to the period without ( $d=0.36$  vs.  $0.03$ ). Both patients and caregivers reported significant improvements in everyday functioning ( $p < .05$ ). There were no further improvements at the four-month follow-up assessment. A comprehensive program of cognitive rehabilitation may improve attention and memory, as well as everyday cognitive functioning, in patients with severe or moderate TBI.

## Improving Everyday Memory Performance After Acquired Brain Injury: An RCT on Recollection and Working Memory Training



Richter KM, Mödden C, Eling P, Hildebrandt H

Online First Publication, April 26, 2018. <http://dx.doi.org/10.1037/neu0000445>

**OBJECTIVE:** To show the effectiveness of a combined recognition and working memory training on everyday memory performance in patients suffering from organic memory disorders.

**METHOD:** In this double-blind, randomized controlled Study 36 patients with organic memory impairments, mainly attributable to stroke, were assigned to either the experimental or the active control group. In the experimental group a working memory training was combined with a recollection training based on the repetition-lag procedure. Patients in the active control group received the memory therapy usually provided in the rehabilitation center. Both groups received nine hours of therapy. Prior (T0) and subsequent (T1) to the therapy, patients were evaluated on an everyday memory test (EMT) as well as on a neuropsychological test battery. Based on factor analysis of the neuropsychological test scores at T0 we calculated

composite scores for working memory, verbal learning and word fluency.

**RESULTS:** After treatment, the intervention group showed a significantly greater improvement for WM performance compared with the active control group. More importantly, performance on the EMT also improved significantly in patients receiving the recollection and working memory training compared with patients with standard memory training.

**CONCLUSION:** Our results show that combining working memory and recollection training significantly improves performance on everyday memory tasks, demonstrating far transfer effects. The present study argues in favor of a process-based approach for treating memory impairments. (PsycINFO Database Record (c) 2018 APA, all rights reserved)

# RehaCom software application is effective in cognitive rehabilitation of patients with brain injuries.

Physical Medicine and Rehabilitation Research

Pantartzidou, A., Dionyssiotis, Y., Stefan, E., Samli, E., Georgiadis, T., & Kandylakis, E. (2017). Physical Medicine and Rehabilitation Research, 2(1).

**OBJECTIVES:** To investigate effectiveness of RehaCom cognitive rehabilitation software compared to creative activities program in neuropsychological parameters in patients with cognitive deficits due to acquired central nervous system disorder.

**BACKGROUND:** Impairment in cognitive function is common in patients with acquired brain injury and influences negatively the rehabilitation outcome.

**METHODS/MEASURES:** The study included 96 subjects with different neurological conditions: cerebrovascular accident, hemiplegia, multiple sclerosis and traumatic brain injury. Fifty-six patients participated in the RehaCom cognitive rehabilitation program. Controls performed a program of creative activities. Both groups participated in a comprehensive rehabilitation program including physical therapy, occupational therapy and psychological support. In admission and at discharge a cognitive skill evaluation was performed in the patients of both groups

based on the Montreal Cognitive Assessment (MoCA) psychometric screening test.

**RESULTS:** The average RehaCom intervention participation time was  $115 \pm 70$  days. It was observed that the treatment group MoCA score upon exit was statistically significantly higher than upon admission in assessment tasks of attention and concentration, reaction behavior, visuo-constructive ability, verbal memory, topological memory, visuo-motor coordination and exploration, compared with the control group ( $p < 0.001$ ). The sub-group that seemed to have derived the most advantage is the cerebrovascular accident-right hemiplegia.

**CONCLUSION:** Computerized cognitive rehabilitation with the RehaCom program results in improvement in cognitive function and can be used as a treatment tool beneficial to patients presenting cognitive impairment.

## Effectiveness of a Computer-Based Training Program of Attention and Memory in Patients with Acquired Brain Damage

 behavioral sciences

Fernandez E, Bergado Rosado JA, Rodriguez Perez D, Salazar Santana S, Torres Aguilar M, Bringas ML. Behav Sci (Basel). 2017 Dec 30;8(1). pii: E4. doi: 10.3390/bs8010004.

Many training programs have been designed using modern software to restore the impaired cognitive functions in patients with acquired brain damage (ABD). The objective of this study was to evaluate the effectiveness of a computer-based training program of attention and memory in patients with ABD, using a two-armed parallel group design, where the experimental group ( $n = 50$ ) received cognitive stimulation using RehaCom software, and the control group ( $n = 30$ ) received the standard cognitive stimulation (non-computerized) for eight weeks. In order to assess the possible cognitive changes after the treatment, a post-pre experimental design was

employed using the following neuropsychological tests: Wechsler Memory Scale (WMS) and Trail Making test A and B. The effectiveness of the training procedure was statistically significant ( $p < 0.05$ ) when it established the comparison between the performance in these scales, before and after the training period, in each patient and between the two groups. The training group had statistically significant ( $p < 0.001$ ) changes in focused attention (Trail A), two subtests (digit span and logical memory), and the overall score of WMS. Finally, we discuss the advantages of computerized training rehabilitation and further directions of this line of work.

Acquired Brain Injury

Neurodegenerative Diseases

Prevention of cognitive Deterioration / Geriatrics

Neurodevelopmental Disorders

Mental Illness

Combination Therapy

## Can impaired working memory functioning be improved by training? A meta-analysis with a special focus on brain injured patients

Neuropsychology

Weicker J, Villringer A, Thöne-Otto A

Neuropsychology. 2016 Feb;30(2):190-212. doi: 10.1037/neu0000227

**OBJECTIVE:** Deficits in working memory (WM) are commonly observed after brain injuries and cause severe impairments in patients' everyday life. It is still under debate if training can enhance or rehabilitate WM in case of malfunction. The current meta-analysis investigates this issue from a clinical point of view. It addresses under which conditions and for which target group WM training may be justifiable.

**METHOD:** Relevant WM training studies were identified by searching electronic literature databases with a comprehensive search term. In total, 103 studies, which added up to 112 independent group comparisons (N = 6,113 participants), were included in the analysis.

**RESULTS:** Overall, WM training caused a moderate and long-lasting improvement in untrained WM tasks. Moreover, improvement of WM functioning led to sustainable better evaluation of everyday life

functioning, however, effect sizes were small. Concerning transfer effects on other cognitive domains, long-lasting improvements with small effect sizes were observed in cognitive control and reasoning/intelligence. In contrast, small immediate, but no long-term effects were found for attention and long-term memory. Studies with brain injured patients demonstrated long-lasting improvements in WM functions with moderate to large effect sizes. A main moderator variable of intervention efficacy is the number of training sessions applied.

**CONCLUSION:** WM training produces long-lasting beneficial effects which are strongly pronounced in patients with acquired brain injuries. This finding supports the application of WM training in clinical settings. To determine optimal training conditions, future studies must systematically investigate the characteristics of interventions as they are at present inevitably confounded.

## Working memory training and semantic structuring improves remembering future events, not past events

Neurorehabilitation  
& Neural Repair

Richter KM, MSc, Mödden C, MSc, Eling P, PhD, Hildebrandt H, Prof.

Neurorehabil Neural Repair. 2015 Jan; 29(1):33-40. doi: 10.1177/1545968314527352. Epub 2014 Apr 2.

**OBJECTIVES:** Memory training in combination with practice in semantic structuring and word fluency has been shown to improve memory performance. This study investigated the efficacy of a working memory training combined with exercises in semantic structuring and word fluency and examined whether training effects generalize to other cognitive tasks.

**METHODS:** In this double-blind randomized control study, 36 patients with memory impairments following brain damage were allocated to either the experimental or the active control condition, with both groups receiving 9 hours of therapy. The experimental group received a computer-based

working memory training and exercises in word fluency and semantic structuring. The control group received the standard memory therapy provided in the rehabilitation center. Patients were tested on a neuropsychological test battery before and after therapy, resulting in composite scores for working memory; immediate, delayed, and prospective memory; word fluency; and attention.

**RESULTS:** The experimental group improved significantly in working memory and word fluency. The training effects also generalized to prospective memory tasks. No specific effect on episodic memory could be demonstrated.



# Effect of computerized cognitive rehabilitation program on cognitive function and activities of living in stroke patients



Yoo C, Yong M, Chung J, Yang, J; Phys Ther Sci. 2015 Aug; 27(8): 2487-2489.  
Published online 2015 Aug 21. doi: 10.1589/jpts.27.2487

**PURPOSE:** The objective of this study was to examine the effect of cognitive rehabilitation using a computer on cognitive function and activities of daily living in stroke patients presenting impairment of cognitive function.

**SUBJECTS:** Forty-six stroke patients were divided into two groups (a training group and control group) through random assignment.

**METHODS:** The training group received rehabilitation therapy and an additional computerized cognitive rehabilitation program using The RehaCom software 30 minutes/day, 5 times/week for 5 weeks. The control group received only rehabilitation therapy including physical and occupational therapy. A comparative analysis on all subjects was

conducted before and after the experiment using a cognitive test and activities of daily living test.

**RESULTS:** After 5 weeks of therapy, the training group presented statistically significant improvement in cognitive function assessment items of digit span, visual span, visual learning, auditory continuous performance, visual continuous performance, and others compared with the control group but did not present statistically significant improvement in activities of daily living.

**CONCLUSION:** It was revealed through this study that computerized cognitive rehabilitation with the RehaCom program results in improvement in cognitive function and can be used as a treatment tool beneficial to stroke patients presenting cognitive impairment.

## Analysis of central mechanism of cognitive training on cognitive impairment after stroke: Resting-state functional magnetic resonance imaging study.



Lin, Z. C., Tao, J., Gao, Y. L., Yin, D. Z., Chen, A. Z., & Chen, L. D. (2014).  
Journal of International Medical Research, 42(3), 659-668.

**OBJECTIVE:** To investigate the central mechanism of cognitive training in patients with stroke, using resting state (RS) functional magnetic resonance imaging (fMRI).

**METHODS:** Patients with stroke and executive function and memory deficit were randomized to receive computer-assisted cognitive training (treatment group; total 60 h training over 10 weeks) or no training (control group). All participants received neuropsychological assessment and RS fMRI at baseline and 10 weeks.

**RESULTS:** Patients in the treatment group (n = 16) showed increased functional connectivity (FC) of the hippocampus with the frontal lobe (right inferior, right

middle, left middle, left inferior and left superior frontal gyrus) and left parietal lobe at 10 weeks compared with baseline. Patients in the control group (n = 18) showed decreased FC of the left hippocampus-right occipital gyrus, and right hippocampus-right posterior lobe of cerebellum and left superior temporal gyrus. Significant correlations were found between improved neuropsychological scores and increased FC of the hippocampus with the frontal lobe and left parietal lobe in the treatment group only.

**CONCLUSIONS:** Increased RS FC of the hippocampus with the frontal and parietal lobes may be an important mechanism of cognitive recovery after stroke.

Acquired  
Brain Injury

Neurodegenerative  
Diseases

Prevention of cognitive  
Deterioration / Geriatrics

Neurodevelopmental  
Disorders

Mental  
Illness

Combination  
Therapy

## Effect of integrated cognitive therapy on hippocampal functional connectivity patterns in stroke patients with cognitive dysfunction: a resting-state fMRI study.

Archives of Physical Medicine and Rehabilitation

Yang, S., Jiang, C., Ye, H., Tao, J., Huang, J., Gao, Y., Lin, Z. & Chen, L. (2014). Evidence-Based Complementary and Alternative Medicine, 2014.

**OBJECTIVE:** This study aimed to identify abnormal hippocampal functional connectivity (FC) following ischemic stroke using resting-state fMRI. We also explored whether abnormal hippocampal FC could be modulated by integrated cognitive therapy and tested whether these alterations were associated with cognitive performance.

**METHODS:** 18 right-handed cognitively impaired ischemic stroke patients and 18 healthy control (HC) subjects were included in this study. Stroke subjects were scanned at baseline and after integrated cognitive therapy, while HCs were only scanned at baseline, to identify regions that show significant correlations with the seed region. Behavioral and cognitive assessments were obtained before each scan.

**RESULTS:** During the resting state, we found abnormal hippocampal FC associated with temporal regions, insular cortex, cerebellum, and prefrontal cortex in stroke patients compared to HCs. After integrated cognitive therapy, however, the stroke group showed increased hippocampal FC mainly located in the prefrontal gyrus and the default mode network (DMN). Altered hippocampal FC was associated with cognitive improvement.

**CONCLUSION:** Resting-state fMRI may provide novel insight into the study of functional networks in the brain after stroke. Furthermore, altered hippocampal FC may be a compensatory mechanism for cognitive recovery after ischemic stroke.

## Clinical Impact of RehaCom Software for Cognitive Rehabilitation of Patients with Acquired Brain Injury

MEDICC Review

Fernández E, Bringas ML, Salazar S, Rodríguez D, García ME, Torres M. MEDICC Rev. 2012 Oct; 14(4):32-5.

We describe the clinical impact of the RehaCom computerized cognitive training program instituted in the International Neurological Restoration Center for rehabilitation of brain injury patients. Fifty patients admitted from 2008 through 2010 were trained over 60 sessions. Attention and memory functions were assessed with a pre- and

post-treatment design, using the Mini-Mental State Examination, Wechsler Memory Scale and Trail Making Test (Parts A and B). Negative effects were assessed, including mental fatigue, headache and eye irritation. The program's clinical usefulness was confirmed, with 100% of patients showing improved performance in trained functions.

# A Randomized Controlled Trial Comparing 2 Interventions for Visual Field Loss With Standard Occupational Therapy During Inpatient Stroke Rehabilitation

Neurorehabilitation  
& Neural Repair

Mödden C, Behrens M, Damke I, Eilers N, Kastrup A, Hildebrandt H

Neurorehabil Neural Repair. 2012 Jun;26 (5):463-9. doi: 10.1177/1545968311425927. Epub 2011 Dec 2.

**BACKGROUND AND PURPOSE:** Compensatory and restorative treatments have been developed to improve visual field defects after stroke. However, no controlled trials have compared these interventions with standard occupational therapy (OT).

**METHODS:** A total of 45 stroke participants with visual field defect admitted for inpatient rehabilitation were randomized to restorative computerized training (RT) using computer-based stimulation of border areas of their visual field defects or to a computer-based compensatory therapy (CT) teaching a visual search strategy. OT, in which different compensation strategies were used to train for activities of daily living, served as standard treatment for the active control group. Each treatment group received 15 single sessions of 30 minutes distributed over 3 weeks. The primary outcome measures were visual

field expansion for RT, visual search performance for CT, and reading performance for both treatments. Visual conjunction search, alertness, and the Barthel Index were secondary outcomes.

**RESULTS:** Compared with OT, CT resulted in a better visual search performance, and RT did not result in a larger expansion of the visual field. Intragroup pre-post comparisons demonstrated that CT improved all defined outcome parameters and RT several, whereas OT only improved one.

**CONCLUSIONS:** CT improved functional deficits after visual field loss compared with standard OT and may be the intervention of choice during inpatient rehabilitation. A larger trial that includes lesion location in the analysis is recommended.

## Attention remediation following traumatic brain injury in childhood and adolescence

Neuropsychology

Galbiati S, Recla M, Pastore V, Liscio M, Bardoni A, Castelli E, Strazzer S

Neuropsychology. 2009 Jan;23(1):40-9. doi: 10.1037/a0013409.

Traumatic brain injury (TBI) frequently affects both the basic and the superordinate components of attention; deficits vary according to patient age. This study evaluated the efficacy of a specific remediation intervention for attention. Sixty-five TBI patients (aged 6-18 years) with attention deficit were assessed at baseline and at 1-year follow-up: 40 patients received attention-specific neuropsychological training for 6 months, and the control group comprised 25 patients. Cognitive assessment included a Wechsler Intelligence Scale (e.g., A. Orsini, 1993) and the Continuous Performance Test II (CPT II; C. K. Conners, 2000). The Vineland Adaptive Behavior

Scales (VABS; S. Sparrow, D. Balla & D. V. Cicchetti, 1984) was administered to assess the treatment's ecological validity. At baseline, all patients presented with a mild intellectual disability and pathological scores on the CPT II. At follow-up, significant differences were found between the 2 groups on the CPT II and VABS: The clinical group improved more than the control group. Specific remediation training for attention, including a combination of a process-specific approach and metacognitive strategies, significantly improved attention performance. Improvement in attention skills also affected adaptive skills positively.

Acquired  
Brain Injury

Neurodegenerative  
Diseases

Prevention of cognitive  
Deterioration / Geriatrics

Neurodevelopmental  
Disorders

Mental  
Illness

Combination  
Therapy

# The Effects of a Computer-assisted Cognition Training Program (RehaCom®) in Stroke Patients



Sung Hun Shin, M.D., Ji Sung Kim, M.D. and Yong Kyun Kim, M.D.

Brain & NeuroRehabilitation Vol. 1, No. 2, September, 2008

**Objective:** To evaluate the effect of computer-assisted cognitive training program (RehaCom®) on cognitive function of the patients with stroke.

**Method:** Fifty seven subjects with stroke (34 males, 23 females) were enrolled and classified into two groups, experimental and control group. There was no significant difference between two groups in age sex and lesion type distribution. Control group received conventional rehabilitation therapy including physical and occupational therapy. Experimental group received additional computer-assisted cognitive training using RehaCom software (Germany, 1996), 5 times per a week, 30 minutes per session, for 4 weeks. The RehaCom software consisted of reaction behavior, memory of words, topological memory programs. All patients were assessed their cognitive function using Computerized Neuropsychological Test (CNT), Lowenstein Occupational Therapy Cognitive Assessment (LOTCA) and Korean Version of Mini-Mental Status Examination (MMSE-K) before and after treatment.

Functional independence measurement (FIM) was also applied for evaluation of functional status.

**Results:** There was no difference between two groups in the LOTCA, CNT and FIM scores at baseline. Four weeks later, scores of the MMSE and FIM were significantly improved in the experimental group compared to the control group ( $p < 0.05$ ). Especially, the improvement was significant in moderate cognitive impairment group (MMSE = 11~21) ( $p < 0.05$ ). In learned patients of experimental group, the score of the MMSE and LOTCA were significantly more improved than control group ( $p < 0.05$ ).

**Conclusion:** Computer-assisted cognitive training would be useful as a additional tool of cognitive rehabilitation in patients with stroke. Especially, the effect of computer-assisted cognitive training program was far better in patients with moderate cognitive impairment and in patients who show learning in cognitive training program.

## Evaluation of a Neuropsychological Training of Attentional Functions for Brain Damaged Outpatients



Eidenmüller A, Kallus KW, Fröhlich H, Bieber K, Poimann H

Zeitschrift für Neuropsychologie (2001), 12, pp. 160-172. <https://doi.org/10.1024//1016-264X.12.2.160>.

Within the scope of an experimental study design the efficacy of an outpatient neuropsychological attention training was studied in 20 patients with different kinds of brain damages. The patients have been divided into two groups: one group received a specific attention training and the other a nonspecific neuropsychological training over a period of eight weeks altogether. Beyond this the attention training group has been divided into the prior trained

attention components (elementary versus higher attentional functions). To scrutinize the efficacy of the training program a number of computer-aided tests, paper-pencil tests and self-assessment measurements have been brought in. After completion of the training program significant training effects could be shown in a wide range of the attention tests. These results could partly be seen in the self-assessment measurement as well.

## Cognitive rehabilitation program to improve cognition of cancer patients treated with chemotherapy: A 3-arm randomized trial.

Cancer

Dos Santos M, Hardy-Léger I, Rigal O, Licaj I, Dauchy S, Levy C, Noal S, Segura C, Delcambre C, Allouache D, Parzy A, Barriere J, Petit T, Lange M, Capel A, Clarisse B, Grellard JM, Lefel J, Joly F. (2020). *Cancer*, 126 (24), 5328-5336.

**BACKGROUND:** There is no treatment for cancer-related cognitive impairment, an important adverse effect that negatively impacts quality of life (QOL). We conducted a 3-arm randomized controlled trial to evaluate the impact of computer-assisted cognitive rehabilitation (CR) on cognition, QOL, anxiety, and depression among cancer patients treated with chemotherapy.

**METHODS:** Patients who reported cognitive complaints during or after completing chemotherapy were randomly assigned to 1 of 3 12-week CR programs: computer-assisted CR with a neuropsychologist (experimental group A), home cognitive self-exercises (active control group B), or phone follow-up (active control group C). Subjective cognition was assessed by the Functional Assessment of Cancer Therapy–Cognitive Function (FACT-Cog), objective cognition was assessed by neuropsychological tests, QOL was assessed by the FACT-General, and depression and anxiety were assessed by psychological tests. The

primary endpoint was the proportion of patients with a 7-point improvement in the FACT-Cog perceived cognitive impairment (PCI) score.

**RESULTS:** Among the 167 enrolled patients (median age, 51 years), group A had the highest proportion of patients with a 7-point PCI improvement (75%), followed by groups B (59%) and C (57%), but the difference was not statistically significant ( $P = .13$ ). Compared with groups B and C, the mean difference in PCI score was significantly higher in group A ( $P = .02$ ), with better perceived cognitive abilities ( $P < .01$ ) and a significant improvement in working memory ( $P = .03$ ). Group A reported higher QOL related to cognition (FACT-Cog QOL) ( $P = .01$ ) and improvement in depression symptoms ( $P = .03$ ).

**CONCLUSIONS:** These results suggest a benefit of a computer-based CR program in the management of cancer-related cognitive impairment and complaints.

## Do Secondary Progressive Multiple Sclerosis patients benefit from Computer-based cognitive neurorehabilitation? A randomized sham controlled trial.



Lambros Messinis, Mary H Kosmidis, Grigorios Nasios, Spyridon Konitsiotis, Aikaterini Ntoskou, Christos Bakirtzis, Nikolaos Grigoriadis, Panayiotis Patrikelis, Elias Panagiotopoulos, Philippos Gourzis, Sonia Malefaki, Panagiotis Papat-  
hanasopoulos. (2020). Multiple Sclerosis and Related Disorders, 39, 101932.

**BACKGROUND:** Cognitive impairment is common in multiple sclerosis (MS), but deficits tend to be more pronounced in progressive MS, negatively impacting daily functional capacity. Despite this, most cognitive rehabilitation (CR) interventions to date have focused on relapsing remitting MS (RRMS). Moreover, information on the efficacy of CR in progressive MS is limited and controversial. The present study investigated the efficacy of a home based, computer assisted cognitive rehabilitation (HBCACR) intervention (RehaCom™ software) exclusively in a Secondary Progressive Multiple Sclerosis (SPMS) sample.

**METHODS:** This was a randomized, multi site, sham controlled trial. Thirty six (36) individuals with SPMS, naïve to the RehaCom software, with cognitive deficits were randomized to the treatment (IG; n= 19) or control group condition (CG; n=17). Treatment with the RehaCom modules consisted of 24 domain and task specific, 45 minute session's over an 8-week period, three sessions per week, applied by each patient at home. The CG completed non specific computer based activities at home with the same frequency and duration. Primary cognitive outcome measures included the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) battery, and secondary outcome measures for depression (BDI-FS), fatigue (MFIS), and quality of life (EuroQol EQ-5D) visual analogue scale (VAS).

**RESULTS:** The two groups were well matched on demographic and clinical characteristics, cognitive reserve and severity of cognitive deficits at baseline assessment. At post treatment assessment the IG group showed significant improvements with large effect sizes; in verbal learning [z = -4.759, p <.0005, g = 2.898], visuospatial memory [z = -3.940, p <.0005, g = 1.699] and information processing speed [z = -4.792, p <.0005, g = 2.980], compared with the sham control group. We also found significant between group differences on physical [z=3.308, p = .001, g= -.604], cognitive [z = -4.011, p <.0005, g = -1.654], psychosocial [z= 3.308, p = .010, g = -.940], and general fatigue impact [z= -2.623, p = .008, g = -.519], depression severity [z = -2.730, p = .006, g = -.519], and quality of life [z= -4.239, p <.0005, g = -1.885] in favor of the treated group.

**CONCLUSION:** These data provide the first evidence supporting the efficacy of computer based restorative cognitive rehabilitation applied at home exclusively in SPMS patients, suggesting that adaptive neuroplasticity may occur after functional cognitive training in progressive MS. Improved cognitive functioning in combination with mood augmentation appear to have ameliorated fatigue, which impacted daily functioning activity and culminated in improved health related quality of life.

# The therapeutic effect of treatment with RehaCom software on verbal performance in patients with multiple sclerosis.



Darestani, A. A., Davarani, M. N., Hassani-Abharian, P., Zarrindast, M. R., & Nasehi, M. (2020). *Journal of Clinical Neuroscience*, 72, 93-97.

Multiple sclerosis (MS) is characterized by central nervous system lesions that lead to neurological dysfunctions including fatigue, depression and anxiety. MS is affecting almost 2.3 million people around the world, with the significant highest prevalence in the North America. MS also affects different cognitive abilities, such as attention, memory and executive functions. Furthermore, a significant impairment in verbal fluency and naming abilities in patients with MS has been reported.

RehaCom, is a software that has improvement effects on cognitive functions. The goal of this research is to investigate the effect of treatment with RehaCom on verbal performance in patients with MS.

To select the participants, 60 patients with MS who referred to our clinic were chosen randomly and divided into Control (n = 30) and Experimental

(n = 30) groups. The participants in the experimental group were treated by RehaCom software for 10 sessions during 5 weeks (2 sessions per week and each session was 1 h).

Controlled Oral Word Association Test (COWAT) and California Verbal Learning Test – Second Edition (CVLT-II), were used to assess verbal performance (verbal fluency, and verbal learning and memory) at weeks 0 (baseline), 5 (post-test) and 10 (follow-up).

The results showed that, treatment with RehaCom improved verbal performance in patient with MS, at both post-test and follow-up stages. In conclusion, treatment with RehaCom cognitive rehabilitation software can improve verbal fluency, and verbal learning and memory in patient with MS, possibly by affecting the brain regions involved in language performance.

## RehaCom rehabilitation training improves a wide-range of cognitive functions in multiple sclerosis patients.



Naeeni Davarani, M., Arian Darestani, A., Hassani-Abharian, P., Vaseghi, S., Zarrindast, M. R., & Nasehi, M. (2020). *Applied Neuropsychology: Adult*, 1-11.

Multiple sclerosis (MS) is a chronic neurodegenerative disease that impairs cognitive performance. Attention, response control, working memory, and processing speed are highly impaired in MS. On the other hand, RehaCom is a computerized software that improves cognitive dysfunctions. In this study, we aimed to investigate the effect of RehaCom on attention, response control, processing speed, working memory, visuospatial skills, and verbal/non-verbal executive functions in MS patients.

Sixty patients were selected randomly and divided into control (n = 30) and experimental (n = 30) groups. Integrated Auditory Visual-2 (IVA-2), Paced Auditory Serial Addition Test (PASAT), Symbol Digit Modalities

Test (SDMT), Judgment of Line Orientation (JLO) and The Delis–Kaplan Executive Function System (DKEFS) were used to assess cognitive functions. Patients in the experimental group were treated by RehaCom for 5 weeks (two 60-min sessions per week). Cognitive performance of all patients in both groups was assessed at weeks 5 and 10 (post-test and followup stages, respectively).

The results showed that RehaCom treatment improved all studied cognitive functions at the post-test stage. This effect also remained at the follow-up stage for some cognitive functions. In conclusion, treatment with RehaCom may have significant therapeutic effects on cognitive dysfunctions in MS patients.

## Influence of RehaCom Therapy on the Improvement of Manual Skills in Multiple Sclerosis Subjects.



Pawlukowska, Wioletta, Dobrowolska, Natalia, Szylińska, Aleksandra, Koziarska, Dorota, Meller, Agnieszka, Rotter, Iwona, & Nowacki, Przemysław. (2020). *Annals of Rehabilitation Medicine*, 44(2), 142-150.

**OBJECTIVE:** To assess the influence of cognitive therapy, in combination with cognitive software, on manual dexterity in individuals with multiple sclerosis (MS).

**METHODS:** The Nine-Hole Peg Test (NHPT) was used to establish the eligibility of individuals with MS for testing and to assess their upper limb performance. In addition to standard upper limb rehabilitation, 20 participants received RehaCom-based visual-motor therapy, administered three times a week in 20-minute routines.

**RESULTS:** A significant relationship was found between the use of manual therapy that utilized the cognitive function platform and the improvement of the non-dominant hand ( $p=0.037$ ). Compared to controls, the experimental group scored higher on the NHPT, when using the dominant hand ( $p=0.007$ ). All members of the experimental group, aged  $\leq 60$  years, needed considerably less time to do the NHPT with the dominant hand ( $p=0.008$ ).

**CONCLUSION:** Application of manual therapy using the cognitive function platform improves performance of the hand. However, further research is needed to analyze the correlation between cognitive function and motor performance in patients with MS.

## The Effects of Cognitive Training on Brain Network Activity and Connectivity in Aging and Neurodegenerative Diseases: a Systematic Review.



van Balkom, T.D., van den Heuvel, O.A., Berendse, H.W. et al. (2020). *Neuropsychol Rev* 30, 267-286

Cognitive training (CT) is an increasingly popular, non-pharmacological intervention for improving cognitive functioning in neurodegenerative diseases and healthy aging. Although meta-analyses support the efficacy of CT in improving cognitive functioning, the neural mechanisms underlying the effects of CT are still unclear. We performed a systematic review of literature in the PubMed, Embase and PsycINFO databases on controlled CT trials ( $N > 20$ ) in aging and neurodegenerative diseases with pre- and post-training functional MRI outcomes up to November 23rd 2018 (PROSPERO registration number CRD42019103662). Twenty articles were eligible for our systematic review. We distinguished between multi-domain and single-domain CT. CT induced both increases and decreases in task-related functional activation, possibly indicative of an inverted U-shaped curve association between regional

brain activity and task performance. Functional connectivity within 'cognitive' brain networks was consistently reported to increase after CT while a minority of studies additionally reported increased segregation of frontoparietal and default mode brain networks. Although we acknowledge the large heterogeneity in type of CT, imaging methodology, in-scanner task paradigm and analysis methods between studies, we propose a working model of the effects of CT on brain activity and connectivity in the context of current knowledge on compensatory mechanisms that are associated with aging and neurodegenerative diseases.

**EFFICACY OF REHACOM SPECIFICALLY** Five studies applied a specific multi-domain training (RehaCom) in individuals with MS with variable length (12-36 h). Using independent component analysis on



resting-state fMRI scans, RehaCom training increased resting-state functional connectivity within the DMN, mainly in the posterior, parieto-occipital DMN regions (Bonavita et al., 2015), which correlated with a lower post-treatment interference on the Stroop task. Another study showed that RehaCom led to increased or stable resting-state activity fluctuations of salience network, FPN, and DMN areas relative to decreased fluctuations in the control group (Filippi et al., 2012). In this study, task-related activation of the dorsolateral prefrontal cortex (dlPFC) and PCC during the interference condition of the Stroop task was also increased, correlating with performance on a working memory task (paced auditory serial addition test), but no information was provided on the direction of these specific correlations. On the same dataset, Parisi and colleagues (Parisi, Rocca,

Valsasina, et al., 2014) reported increased resting-state functional connectivity between the anterior cingulate cortex (ACC) and inferior parietal lobe after RehaCom training that was related to improved performance on a working memory task.

RehaCom training in MS induced increased task-related activation during a working memory task of a temporo-parietal region (Campbell et al., 2016), and in the superior parietal and posterior cerebellar lobe; the latter correlated positively with post-training Stroop interference task performance (lobe VI; Cerasa et al., 2013). After a 12-week follow-up period, task-related activity of the temporal-parietal and additional frontal and prefrontal regions was still higher compared with the control group (Campbell et al., 2016).

## Efficacy of computer-based cognitive training in neuropsychological performance of patients with multiple sclerosis: A systematic review and meta-analysis



Dardiotis E, Nousia A, Siokas V, Tsouris Z, Andravizou A, Mentis AA, Florou D, Messinis L, Nasios G. *Mult Scler Relat Disord.* 2018 Feb; 20:58-66.

**IMPORTANCE:** Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system characterized by relapses and a progressive course that may lead to accumulation of physical and cognitive disability. Cognitive training interventions seem to improve the cognitive performance of MS patients. The aim of the present meta-analysis is to quantitatively investigate the effect of computer-based cognitive rehabilitation on the neuropsychological performance of patients with MS.

**METHODS:** We performed a systematic review of the PubMed database to identify available studies that performed computer-based cognitive training in MS patients. Studies should have reported pre- and post-cognitive training neuropsychological tests scores and included both intervention and placebo/ no-intervention MS groups. We analyzed the effect of computer-based cognitive rehabilitation on individual neuropsychological tests, on specific functional domains, and on overall cognition performance. The effect-size of cognitive training pre- and post-treatment compared to placebo/ no-intervention was

estimated using the standardized mean difference (SMD). The 95% confidence intervals (CI) were estimated using a Z test by comparing the final values. Baseline between-group differences in selected outcomes were estimated with ANOVA.

**RESULTS:** In total, 9 studies fulfilled the criteria for inclusion and were inserted in the quantitative analysis. Computer-based cognitive training was found to improve the performance in the memory domain of MS patients compared to control interventions (SMD, 0.22; 95% CI 0.01-0.43;  $p = 0.04$ ). Moreover, in the subgroup analysis, cognitive training demonstrated significant effects in Selective Reminding Test (SRT) delay memory (SMD, 0.58; 95% CI 0.29-0.87;  $p < 0.001$ ).

**CONCLUSIONS:** The present meta-analysis revealed a significant effect for computer-based cognitive training on the performance of the memory domain of patients with MS. This finding may have significant implications in the current treatment practice when cognitive decline is detected in MS patients.

# Evidenced-Based Cognitive Rehabilitation for Persons with Multiple Sclerosis: An Updated Review of the Literature from 2007 to 2016.

Goverover Y, Chiaravalloti ND, O'Brien AR, DeLuca J. Arch Phys Med Rehabil. 2018 Feb;99(2):390-407. doi: 10.1016/j.apmr.2017.07.021. Epub 2017 Sep 25. PMID: 28958607.

**OBJECTIVE:** To update the clinical recommendations for cognitive rehabilitation of people with multiple sclerosis (MS), based on a systematic review of the literature from 2007 through 2016.

**DATA SOURCES:** Searches of MEDLINE, PsycINFO, and CINAHL were conducted with a combination of the following terms: attention, awareness, cognition, cognitive, communication, executive, executive function, language, learning, memory, perception, problem solving, reasoning, rehabilitation, remediation, training, processing speed, and working memory. One hundred twenty-nine articles were identified and underwent initial screening.

**STUDY SELECTION:** Fifty-nine articles were selected for inclusion after initial screening. Nineteen studies were excluded after further detailed review. Forty studies were fully reviewed and evaluated.

**DATA EXTRACTION:** Articles were assigned to 1 of 6 categories: attention, learning and memory, processing speed and working memory, executive functioning, metacognition, or nonspecified/combined cognitive domains. Articles were abstracted and levels of evidence were decided using specific criteria.

**DATA SYNTHESIS:** The current review yielded 6 class I studies, 10 class II studies, and 24 class III studies. One intervention in the area of verbal learning and memory received support for a practice standard, 2 computer programs received support as practice guidelines (in the area of attention and multicognitive

domains), and several studies provided support for 5 practice options in the domains of attention and learning and memory.

**CONCLUSIONS:** Substantial progress has been made since our previous review regarding the identification of effective treatments for cognitive impairments in persons with MS. However, much work remains to be done to optimize rehabilitation potential by applying the most methodologically rigorous research designs to provide class I evidence in support of a given treatment strategy.

**EFFICACY OF REHACOM SPECIFICALLY:** „Purely computer-based treatments have clearly increased in popularity, likely because of the wide availability of technology and recent technologic advances. Specifically, 5 studies (1 class I study, 1 class II study, and 3 class III studies) examined the efficacy of the RehaCom program. Significant improvements were found in attention and executive functions, with brain changes noted, and sustained effects over time.“ (p. 404)

**RECOMMENDATIONS:** „Three studies used the RehaCom to treat multiple domains of cognition, with 1 providing class II evidence and 2 providing class III evidence. All 3 studies showed promising results. Although RehaCom can be recommended as a practice guideline at this point, more class I studies are needed to provide a recommendation for practice standard.“ (p. 403)

# Efficacy of a Computer-Assisted Cognitive Rehabilitation Intervention in Relapsing-Remitting Multiple Sclerosis Patients: A Multicenter Randomized Controlled Trial

BEHAVIOURAL  
NEUROLOGY

Messinis L, Nasios G, Kosmidis MH, Zampakis P, Malefaki S, Ntoskou K, Nousia A, Bakirtzis C, Grigoriadis N, Gourzis P, Papathanasopoulos P; Behavioural Neurology, Vol. 2017, Article ID 5919841, doi.org/10.1155/2017/5919841

Cognitive impairment is frequently encountered in multiple sclerosis (MS) affecting between 40–65% of individuals, irrespective of disease duration and severity of physical disability. In the present multicenter randomized controlled trial, fifty-eight clinically stable RRMS patients with mild to moderate cognitive impairment and relatively low disability status were randomized to receive either computer-assisted (RehaCom) functional cognitive training with an emphasis on episodic memory, information processing speed/attention, and executive functions for 10 weeks (IG;  $n = 32$ ) or standard clinical care (CG;  $n = 26$ ). Outcome measures included a flexible comprehensive neuropsychological battery of tests sensitive to MS patient deficits and feedback regarding personal benefit gained from the

intervention on four verbal questions. Only the IG group showed significant improvements in verbal and visuospatial episodic memory, processing speed/attention, and executive functioning from pre- to postassessment. Moreover, the improvement obtained on attention was retained over 6 months providing evidence on the longterm benefits of this intervention. Group by time interactions revealed significant improvements in composite cognitive domain scores in the IG relative to the demographically and clinically matched CG for verbal episodic memory, processing speed, verbal fluency, and attention. Treated patients rated the intervention positively and were more confident about their cognitive abilities following treatment.

## A Randomised Controlled Trial of Efficacy of Cognitive Rehabilitation in Multiple Sclerosis: A Cognitive, Behavioural, and MRI Study



Campbell J, Langdon D, Cercignani M, Rashid W

Hindawi Publishing Corporation Neural Plasticity Volume 2016, Article ID 4292585, 9 pages

**AIM:** To explore the efficacy of home-based, computerised, cognitive rehabilitation in patients with multiple sclerosis using neuropsychological assessment and advanced structural and functional magnetic resonance imaging (fMRI).

**METHODS:** 38 patients with MS and cognitive impairment on the Brief International Cognitive Assessment for MS (BICAMS) were enrolled. Patients were randomised to undergo 45 minutes of computerized cognitive rehabilitation using RehaCom software ( $n = 19$ ) three times weekly for six weeks or to a control condition ( $n = 19$ ). Neuropsychological and MRI data were obtained at baseline (time1), following the 6-week intervention (time 2), and after a further twelve weeks (time 3). Cortical activations were explored using fMRI

and microstructural changes were explored using quantitative magnetization transfer (QMT) imaging.

**RESULTS:** The treatment group showed a greater improvement in SDMT gain scores between baseline and time 2 compared to the control group ( $p = 0.005$ ). The treatment group exhibited increased activation in the bilateral prefrontal cortex and right temporoparietal regions relative to control group at time 3 ( $p < 0.05$ FWE corrected). No significant changes were observed on QMT.

**CONCLUSION:** This study supports the hypothesis that home-based, computerised, cognitive rehabilitation may be effective in improving cognitive performance in patients with MS.

Acquired  
Brain Injury

Neurodegenerative  
Diseases

Prevention of cognitive  
Deterioration / Geriatrics

Neurodevelopmental  
Disorders

Mental  
Illness

Combination  
Therapy

# Two Years Follow up of Domain Specific Cognitive Training in Relapsing Remitting Multiple Sclerosis: A Randomized Clinical Trial



Mattioli F, Bellomi F, Stampatori C, Provinciali L, Compagnucci L, Uccelli A, Pardini M, Santuccio G, Fregonese G, Pattini M, Allegri B, Clerici R, Lattuada A, Montomoli C, Corso B, Gallo P, Riccardi A, Ghezzi A, Roscio M, Tola MR, Calanca C, Baldini D, Trafficante D, Capra R; *Front Behav Neurosci*. 2016 Feb 23;10:28. doi: 10.3389/fnbeh.2016.00028.

Cognitive rehabilitation in multiple sclerosis (MS) has been reported to induce neuropsychological improvements, but the persistence of these effects has been scarcely investigated over long follow ups. Here, the results of a multicenter randomized clinical trial are reported, in which the efficacy of 15 week domain specific cognitive training was evaluated at 2 years follow up in 41 patients. Included patients were randomly assigned either to domain specific cognitive rehabilitation, or to aspecific psychological intervention. Patients who still resulted to be cognitively impaired at 1 year follow up were resubmitted to the same treatment, whereas the recovered ones were not. Neuropsychological tests and functional scales were administered at 2 years follow up to all the patients. Results revealed that both at 1 and at 2 years follow up more patients in the aspecific group

(18/19, 94% and 13/17, 76% respectively) than in the specific group (11/22, 50% and 5/15, 33% respectively) resulted to be cognitively impaired. Furthermore patients belonging to the specific group showed significantly less impaired tests compared with the aspecific group ones ( $p = 0.02$ ) and a significant amelioration in the majority of the tests. On the contrary patients in the aspecific group did not change. The specific group subjects also perceived a subjective improvement in their cognitive performance, while the aspecific group patients did not. These results showed that short time domain specific cognitive rehabilitation is a useful treatment for patients with MS, shows very long lasting effects, compared to aspecific psychological interventions. Also subjective cognitive amelioration was found in patients submitted to domain specific treatment after 2 years.

## A RCT comparing specific intensive cognitive training to aspecific psychological intervention in RRMS: the SMICT study



Mattioli F, Stampatori C, Bellomi F, Danni M, Compagnucci L, Uccelli A, Pardini M, Santuccio G, Fregonese G, Pattini M, Allegri B, Clerici R, Lattuada A, Montomoli C, Corso B, Capra R. *Front Neurol*. 2015 Jan 13;5:278. doi: 10.3389/fneur.2014.00278. eCollection 2014.

**BACKGROUND:** Specific cognitive rehabilitation in multiple sclerosis (MS) resulted to be effective compared to no treatment. So far the possible role of an aspecific psychological intervention on cognition has not been investigated.

**OBJECTIVE:** The aim of the SMICT RCT was to compare the efficacy of a specific cognitive training with an aspecific psychological intervention in relapsing-remitting MS patients.

**METHODS:** From a sample of 150 patients, with the same disability and immunomodulatory therapy, submitted to neuropsychological examination, 45 impaired in at least one test were included and 41 randomized to have either a specific cognitive training for the impaired function (22) or to an aspecific psychological intervention (19) for 4 months, starting after baseline examination. Neuropsychological tests and functional scales were administered at baseline and 1 year later.

**RESULTS:** After 1 year, the mean number of pathological tests was significantly lower in the specific treatment group, compared to the aspecific group. Memory and attention/speeded information processing functions were mostly improved. Depression and quality of life were not different between groups at follow up.

**CONCLUSION:** Our study demonstrates that an intensive and domain specific cognitive approach results to be more effective than aspecific psychological intervention in patients with MS.

## Cognitive Rehabilitation in Multiple Sclerosis: The Role of Plasticity

 **frontiers**  
in Behavioral Neuroscience

Chiaravalloti ND, Genova HM, DeLuca J

Front Neurol. 2015; 6: 67. Published online 2015 Apr 2. doi: 10.3389/fneur.2015.00067

Cognitive deficits are common in multiple sclerosis (MS), documented at many stages of the disease. Both structural and functional neuroimaging have demonstrated a relationship with cognitive abilities in MS. Significant neuroplasticity of cognitive functions in individuals with MS is evident. Homologous region adaptation, local activation expansion, and extra-region recruitment all occur in an effort to maintain cognitive functioning. While much of this neuroplasticity is adaptive, it may also be maladaptive, particularly in individuals that are demonstrating significant cognitive impairment and/or with disease progression. This maladaptive neuroplasticity may come at the cost of other cognitive functions. Studies of cognitive rehabilitation efficacy have also recently applied neuroimaging techniques to establish outcome. Researchers have

successfully applied various neuroimaging techniques to study the effects of cognitive rehabilitation in MS including task-based fMRI and resting state functional connectivity across multiple realms of cognition including episodic memory, executive functioning, attention, and processing speed. These studies have demonstrated neuroplasticity in the brains of persons with MS through the documentation of changes at the level of the cerebral substrate from before to after non-invasive, non-pharmacological, behavioral treatment for deficits in cognition. Future research should seek to identify adaptive versus maladaptive neuroplasticity associated with specific cognitive rehabilitation programs within all MS phenotypes to foster the validation of the most effective cognitive rehabilitation interventions for persons with MS.

## Cognitive rehabilitation correlates with the functional connectivity of the anterior cingulate cortex in patients with multiple sclerosis.

 **Brain Imaging and Behavior**

Parisi, L., Rocca, M. A., Valsasina, P., Panicari, L., Mattioli, F., & Filippi, M. (2014).

Brain Imaging and Behavior, 8(3), 387-393.

We investigated how resting state (RS) functional connectivity (FC) of the anterior cingulate cortex (ACC) correlates with cognitive rehabilitation in relapsing remitting multiple sclerosis (RRMS) patients. A neuropsychological assessment and RS fMRI at baseline and after 12 weeks were obtained from 20 RRMS patients, who were assigned randomly to undergo

treatment (n=10) (treatment group-TG), which entailed computer-assisted cognitive rehabilitation of attention/information processing and executive functions for 3 days/week, or not to receive any cognitive rehabilitation (n=10) (control group-CG). Voxel-wise changes of ACC RS FC were assessed using SPM8. In both groups, at the two study time

Acquired  
Brain Injury

Neurodegenerative  
Diseases

Prevention of cognitive  
Deterioration / Geriatrics

Neurodevelopmental  
Disorders

Mental  
Illness

Combination  
Therapy

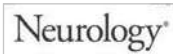
points, ACC activity was correlated with the bilateral middle and inferior frontal gyrus, basal ganglia, posterior cingulate cortex, cerebellum, precuneus, middle temporal gyrus, and inferior parietal lobule (IPL).

At follow up, compared to baseline, the TG showed an increased FC of the ACC with the right middle frontal gyrus (MFG) and right IPL, while the CG showed a decreased FC of the ACC with the right cerebellum and right inferior temporal gyrus (ITG). A significant "treatment × time" interaction was found for the

increased FC of the right IPL and for the decreased FC of the right ITG. In the TG only, significant correlations ( $p < 0.001$ ) were found between improvement of PASAT performance and RS FC of the ACC with the right MFG ( $r = 0.88$ ) and right IPL ( $r = 0.76$ ).

In MS, cognitive rehabilitation correlates with changes in RS FC of brain regions subserving the trained functions. fMRI might be useful to monitor rehabilitative strategies in MS.

## Computer-aided cognitive rehabilitation improves cognitive performances and induces brain functional connectivity changes in relapsing remitting multiple sclerosis patients: an exploratory study



Bonavita S1, Sacco R, Della Corte M, Esposito S, Sparaco M, d'Ambrosio A, Docimo R, Bisecco A, Lavorgna L, Corbo D, Cirillo S, Gallo A, Esposito F, Tedeschi G.

JOURNAL OF NEUROLOGY · October 2014 doi: 10.1007/s00415-014-7528-z. Epub 2014 Oct 12.

To better understand the effects of short-term computer-based cognitive rehabilitation (cCR) on cognitive performances and default mode network (DMN) intrinsic functional connectivity (FC) in cognitively impaired relapsing remitting (RR) multiple sclerosis (MS) patients. Eighteen cognitively impaired RRMS patients underwent neuropsychological evaluation by the Rao's brief repeatable battery and resting-state functional magnetic resonance imaging to evaluate FC of the DMN before and after a short-term (8 weeks, twice a week) cCR. A control group of 14 cognitively impaired RRMS patients was assigned to an aspecific cognitive training (aCT), and underwent the same study protocol. Correlations between DMN and cognitive performances were also tested. After cCR, there was a significant improvement of the following tests: SDMT ( $p < 0.01$ ), PASAT 3" ( $p < 0.00$ ), PASAT 2" ( $p < 0.03$ ), SRT-D ( $p < 0.02$ ), and 10/36 SPART-D ( $p < 0.04$ ); as well as a significant increase of the FC of the DMN in the posterior cingulate cortex (PCC) and bilateral inferior

parietal cortex (IPC). After cCR, a significant negative correlation between Stroop Color-Word Interference Test and FC in the PCC emerged. After aCT, the control group did not show any significant effect either on FC or neuropsychological tests. No significant differences were found in brain volumes and lesion load in both groups when comparing data acquired at baseline and after cCR or aCT. In cognitively impaired RRMS patients, cCR improves cognitive performances (i.e., processing speed and visual and verbal sustained memory), and increases FC in the PCC and IPC of the DMN. This exploratory study suggests that cCR may induce adaptive cortical reorganization favoring better cognitive performances, thus strengthening the value of cognitive exercise in the general perspective of building either cognitive or brain reserve.

# Multiple sclerosis: effects of cognitive rehabilitation on structural and functional MR imaging measures – an explorative study.



Filippi, M., Riccitelli, G., Mattioli, F., Capra, R., Stampatori, C., Pagani, E., ... & Rocca, M. A. (2012). *Radiology*, 262(3), 932-940.

**PURPOSE:** To evaluate brain changes after cognitive rehabilitation in patients with clinically stable relapsing-remitting (RR) multiple sclerosis (MS) by using neuropsychologic assessment and structural and functional magnetic resonance (MR) imaging techniques.

**MATERIALS AND METHODS:** The study was conducted with approval of the involved institutional review boards. Written informed consent was obtained from each participant. Twenty patients with RR MS and cognitive deficits at baseline were randomly assigned to undergo treatment (n = 10), which entailed computer-assisted cognitive rehabilitation of attention and information processing and executive functions, or to serve as a control subjects (n = 10) without cognitive rehabilitation. All patients underwent a standardized neuropsychologic assessment and MR imaging at baseline and after 12 weeks. Changes in gray matter (GM) volumes on three-dimensional T1-weighted images and changes in normal-appearing white matter (NAWM) architecture on diffusion-weighted images were assessed. Changes in functional activity at functional MR imaging during

the Stroop task and at rest were also investigated by using linear models.

**RESULTS:** As compared with their performance at baseline, the patients in the treatment group improved at tests of attention and information processing and executive functions. Neither structural modifications to GM volume nor modifications to NAWM architecture were detected at follow-up in both groups. Functional MR imaging demonstrated modifications of the activity of the posterior cingulate cortex (PCC)/precuneus and dorsolateral prefrontal cortex (PFC) during the Stroop task, as well as modifications of the activity of the anterior cingulum, PCC and/or precuneus, left dorsolateral PFC, and right inferior parietal lobule at rest in the treatment group compared with the control group. In the treatment group, functional MR imaging changes were correlated with cognitive improvement (P= .0001 to .01).

**CONCLUSION:** Rehabilitation of attention and information processing and executive functions in RR MS may be effected through enhanced recruitment of brain networks subserving the trained functions.

## Persistence of the effects of attention and executive functions intensive rehabilitation in relapsing remitting multiple sclerosis



Mattioli F, Stampatori C, Scarpazza C, Parrinello G, Capra R. *Multiple Sclerosis and Related Disorders* 2012 Oct;1(4):168-73. doi: 10.1016/j.msard.2012.06.004.

**BACKGROUND:** Neuropsychological rehabilitation efficacy in multiple sclerosis (MS) is a currently investigated issue. We reported, in a single blind controlled study, that an intensive short duration cognitive training of attention and executive functions significantly improves the treated functions and reduces depression in MS. The persistence of these effects over time are unknown.

**OBJECTIVE:** To evaluate the persistence over time of neuropsychological improvement due to cognitive training nine months after rehabilitation onset.

**METHODS:** This is a single blind randomized controlled study. 24 MS patients were randomly assigned to experimental group (n=13) and received PC assisted neuropsychological treatment for three months, or to control group (n=11), receiving no treatment.

Patients were submitted to neuropsychological evaluation, depression and quality of life questionnaires at baseline, three months and nine months later.

**RESULTS:** Nine months follow up compared to baseline evaluation shows a statistically significant improvement ( $p < 0.05$ ) in attention, information processing and executive functions tests (PASAT 3<sup>+</sup>, COWA/S, WCSTpe), in depression and quality of life questionnaires in rehabilitated patients only.

reliable change index (RCI) and modified RCI confirmed the clinical significance of this improvement in rehabilitated patients.

**CONCLUSIONS:** Three months intensive neuropsychological rehabilitation of attention, information processing and executive functions induces a long lasting and clinically relevant neuropsychological improvement over time and a persistent depression and quality of life amelioration in patients with RR MS.

## Computer-Assisted Cognitive Rehabilitation of Attention Deficits for Multiple Sclerosis: A Randomized Trial With fMRI Correlates



Cerasa A, Gioia MC, Valentino P, Nisticò R, Chiriaco C, Pirritano D, Tomaiuolo F, Mangone G, Trotta M, Talarico T, Bilotti G, Quattrone A.; Neurorehabil Neural Repair. **2013** May; 27(4):284-95. doi: 10.1177/1545968312465194. Epub **2012** Nov 27.

**BACKGROUND:** Although a growing body of evidence has highlighted the role of cognitive rehabilitation (CR) in the management of cognitive dysfunctions in multiple sclerosis (MS), there is still no evidence for a validated therapeutic approach.

**OBJECTIVE:** We propose a new therapeutic strategy characterized by a computer-based intensive attention training program in MS patients with predominant attention deficits. We aim to investigate the effectiveness of our rehabilitation procedure, tailored for those with impaired abilities, using functional magnetic resonance imaging (fMRI).

**METHODS:** Using a double-blind randomized controlled study, we enrolled 12 MS patients, who underwent a CR program (experimental group), and 11 age-gender-matched MS patients, who underwent a placebo intervention (control group). fMRI was recorded during the execution of a cognitive task broadly used

for assessing attention abilities in MS patients (paced visual serial addition test).

**RESULTS:** Significant effects were detected both at a phenotypic and at an intermediate phenotypic level. After CR, the experimental group, in comparison with the control group, showed a specific enhanced performance in attention abilities as assessed by the Stroop task with an effect size of 0.88, which was associated with increased activity in the posterior cerebellar lobule and in the superior parietal lobule.

**CONCLUSIONS:** Our study demonstrates that intensive CR tailored for those with impaired abilities affects neural plasticity and improves some aspects of cognitive deficits in MS patients. The reported neurophysiological and behavioral effects corroborate the benefits of our therapeutic approach, which might have a reliable application in the clinical management of cognitive deficits in MS.

## Cognitive Rehabilitation in Multiple Sclerosis



Barbosa F, Sousa C, Nogueira-Silva L, José Sá M  
Sinapse, Vol. 11, No. 1, May **2011**

**BACKGROUND:** Recent studies have shown that 45%-65% of MS patients have deficits in the cognitive function area that contributes to a significant decrease in their quality of life. Through cognitive

assessment is possible the early identification and subsequent planning of rehabilitation and follow up of cognitive deficits in these patients. In order to improve health care in their cognition, cognitive



rehabilitation uses different techniques and strategies integrating a dynamic process of restoration for a highest level of performance in their physical, psychological and social life.

**PURPOSE:** The main aim of this work is to evaluate the success of cognitive rehabilitation in MS patients with cognitive impairment.

**METHODS:** 28 patients (20 females, 8 males), with diagnosis of mild to moderate (<25) cognitive impairment, with indication for immunomodulatory therapy followed in the MS Clinic of a University Hospital, are part of this study. At first, the cognitive function of these patients was assessed using the Neuropsychological Test battery for MS (Rao et al., 1991) as a composite screening tool of the major cognitive areas. Subsequently, patients underwent weekly sessions for a period of 12 months on a program of cognitive rehabilitation: the RehaCom, an

instrument consisting of several software programs for different areas: attention and concentration, topology memories, reactive behavior and verbal memory. After the completion of the cognitive rehabilitation program, the effectiveness of the whole process was assessed through a new evaluation with above battery of tests comparing the previous results as a pre-post design methodology.

**RESULTS:** Significant improvements in cognitive functions after cognitive rehabilitation program were acquired. The cognitive area with major improvements was the spatial memory.

**DISCUSSION:** This study demonstrates that cognitive rehabilitation, preceded by the neuropsychological evaluation, is an important tool in MS because it may stabilize or enhance improvements in cognitive deficits and thereby improve the quality of life for patients.

## Efficacy and specificity of intensive cognitive rehabilitation of attention and executive functions in multiple sclerosis.



Flavia, M., Stampatori, C., Zanotti, D., Parrinello, G., & Capra, R. (2010).  
Journal of the neurological sciences, 288(1-2), 101-105.

**OBJECTIVE:** To evaluate the efficacy of a computer-based intensive training program of attention, information processing and executive functions in patients with clinically-stable relapsing–remitting (RR) multiple sclerosis (MS) and low levels of disability.

**DESIGN, PATIENTS AND INTERVENTIONS:** A total of 150 patients with RR MS and an Expanded Disability Status Scale (EDSS) score of  $\leq 4$  were examined. Information processing, working memory and attention were assessed by the Paced Auditory Serial Addition Test (PASAT) and executive functions by the Wisconsin Card Sorting Test (WCST). Twenty patients who scored below certain cut-off measures in both tests were included in this double-blind controlled study. Patients were casually assigned to a study group (SG) or a control group (CG) and underwent neuropsychological evaluation at baseline and after 3 months. Patients in the SG received intensive computer-assisted cognitive rehabilitation of attention,

information processing and executive functions for 3 months; the CG did not receive any rehabilitation.

**SETTING:** Ambulatory patients were sent by the MS referral center. Outcome measures: Improvement in neuropsychological test and scale scores.

**RESULTS:** After rehabilitation, only the SG significantly improved in tests of attention, information processing and executive functions (PASAT 3"  $p = 0.023$ , PASAT 2"  $p = 0.004$ , WCSTe  $p = 0.037$ ), as well as in depression scores (MADRS  $p = 0.01$ ). Neuropsychological improvement was unrelated to depression improvement in regression analysis.

**CONCLUSIONS:** Intensive neuropsychological rehabilitation of attention, information processing and executive functions is effective in patients with RR MS and low levels of disability, and also leads to improvement in depression.

# Efficacy and Specificity of intensive cognitive Rehabilitation of Attention and executive Functions in Multiple Sclerosis



Mattioli F, Stampatori C, Zanotti D, Parrinello G, Capra R

J Neurol Sci. 2010 Jan 15; 288(1-2):101-5. doi: 10.1016/j.jns.2009.09.024. Epub 2009 Oct 13.

**OBJECTIVE:** To evaluate the efficacy of a computer-based intensive training program of attention, information processing and executive functions in patients with clinically-stable relapsing-remitting (RR) multiple sclerosis (MS) and low levels of disability.

**DESIGN, PATIENTS AND INTERVENTIONS:** A total of 150 patients with RR MS and an Expanded Disability Status Scale (EDSS) score of  $<$  or  $=$  4 were examined. Information processing, working memory and attention were assessed by the Paced Auditory Serial Addition Test (PASAT) and executive functions by the Wisconsin Card Sorting Test (WCST). Twenty patients who scored below certain cut-off measures in both tests were included in this double-blind controlled study. Patients were casually assigned to a study group (SG) or a control group (CG) and underwent neuropsychological evaluation at baseline and after 3 months. Patients in the SG received intensive computer-assisted cognitive rehabilitation of attention, information processing and executive functions for

3 months; the CG did not receive any rehabilitation.

**SETTING:** Ambulatory patients were sent by the MS referral center.

**OUTCOME MEASURES:** Improvement in neuropsychological test and scale scores.

**RESULTS:** After rehabilitation, only the SG significantly improved in tests of attention, information processing and executive functions (PASAT 3"  $p=0.023$ , PASAT 2"  $p=0.004$ , WCSTe  $p=0.037$ ), as well as in depression scores (MADRS  $p=0.01$ ). Neuropsychological improvement was unrelated to depression improvement in regression analysis.

**CONCLUSIONS:** Intensive neuropsychological rehabilitation of attention, information processing and executive functions is effective in patients with RR MS and low levels of disability, and also leads to improvement in depression.

## Computer-assisted memory retraining of patients with multiple sclerosis



Mendozzi L, Pugnetti L, Motta A, Barbieri E, Gambini A, Cazzullo CL

The Italian Journal of Neurological Sciences; November 1998, Volume 19, Supplement 6, pp S431-S43

This study aimed to assess the efficacy and specificity of direct computer-assisted memory retraining (CR) in MS patients, in comparison to non-specific retraining, while controlling for severity of impairment, psychiatric symptoms and retest effects.

Sixty patients with definite MS and a stable clinical condition were selected. All were assessed neuropsychologically and divided into three matched groups. One group received an 8-week specific CR programme (SCRIP) and another received a non-specific 8-week CR programme (NCRIP) to retrain attention; a third (control) group received no treatment. After

the programmes were completed, all patients were reexamined with the same test battery.

Patients were impaired on all 11 memory and attention tests at baseline. Those who received SCRIP improved on 7 memory outcome measures, compared to only 1 in the NCRIP group and none in the control group. Attention training had no significant effect on relevant outcome measures. Some non-retrained patients showed deterioration of cognitive performance at retest. These results indicate that direct memory training in MS patients is effective in the short-term and is specific. In selected cases, benefits extended to everyday life activities.

Metaanalysis

## Cognitive training in Parkinson disease: A systematic review and meta-analysis



Leung IH, Walton CC, Hallock H, Lewis SJ, Valenzuela M, Lampit A  
Neurology published online October 30, 2015 DOI 10.1212/WNL.0000000000002145

**OBJECTIVE:** To quantify the effects of cognitive training (CT) on cognitive and behavioral outcome measures in patients with Parkinson disease (PD).

**METHODS:** We systematically searched 5 databases for randomized controlled trials (RCTs) of CT in patients with PD reporting cognitive or behavioral outcomes. Efficacy was measured as standardized mean difference (Hedges *g*) of post-training change.

**RESULTS:** Seven studies encompassing 272 patients with Hoehn & Yahr Stages 1–3 were included. The overall effect of CT over and above control conditions was small but statistically significant (7 studies:  $g = 0.23$ , 95 % confidence interval [CI] 0.014–0.44,  $p = 0.037$ ). True heterogeneity across studies was low ( $I^2 = 0\%$ ) and there was no evidence of publication bias. Larger effect sizes were noted on working

memory (4 studies:  $g = 0.74$ , CI 0.32–1.17,  $p = 0.001$ ), processing speed (4 studies:  $g = 0.31$ , CI 0.01–0.61,  $p = 0.04$ ), and executive function (5 studies:  $g = 0.30$ , CI 0.01–0.58,  $p = 0.042$ ), while effects on measures of global cognition (4 studies), memory (5 studies), visuospatial skills (4 studies), and depression (5 studies), as well as attention, quality of life, and instrumental activities of daily living (3 studies each), were not statistically significant. No adverse events were reported.

**CONCLUSIONS:** Though still small, the current body of RCT evidence indicates that CT is safe and modestly effective on cognition in patients with mild to moderate PD. Larger RCTs are necessary to examine the utility of CT for secondary prevention of cognitive decline in this population.

## Neurofunctional correlates of attention rehabilitation in Parkinson's disease: an explorative study.



Cerasa, A., Gioia, M. C., Salsone, M., Donzuso, G., Chiriaco, C., Realmuto, S., ... & Zappia, M. (2014).  
Neurological Sciences, 35(8), 1173-1180.

The effectiveness of cognitive rehabilitation (CR) in Parkinson's disease (PD) is in its relative infancy, and nowadays there is insufficient information to support evidence-based clinical protocols. This study is aimed at testing a validated therapeutic strategy characterized by intensive computer-based attention-training program tailored to attention deficits. We further investigated the presence of synaptic plasticity by means of functional magnetic resonance imaging (fMRI). Using a randomized controlled study, we enrolled eight PD patients who underwent a CR program (Experimental group) and seven clinically/

demographically-matched PD patients who underwent a placebo intervention (Control group). Brain activity was assessed using an 8-min resting state (RS) fMRI acquisition. Independent component analysis and statistical parametric mapping were used to assess the effect of CR on brain function.

Significant effects were detected both at a phenotypic and at an intermediate phenotypic level. After CR, the Experimental group, in comparison with the Control group, showed a specific enhanced performance in cognitive performance as assessed by the

SDMT and digit span forward. RS fMRI analysis for all networks revealed two significant groups (Experimental vs Control) 9 time (T0 vs T1) interaction effects on the analysis of the attention (superior parietal cortex) and central executive neural networks (dorsolateral prefrontal cortex).

We demonstrated that intensive CR tailored for the impaired abilities impacts neural plasticity and improves some aspects of cognitive deficits of PD patients. The reported neurophysiological and behavioural effects corroborate the benefits of our therapeutic approach, which might have a reliable application in clinical management of cognitive deficits.

# Mild Cognitive Impairment (MCI)

## Beneficial effect of computer-based multidomain cognitive training in patients with mild cognitive impairment.



Nousia, A., Martzoukou, M., Siokas, V., Aretouli, E., Aloizou, A. M., Folia, V., ... & Dardiotis, E. (2019).  
Applied Neuropsychology: Adult, 1-10.

The purpose of the present study was to explore the effects of computer-based multidomain cognitive training program on Greek patients with Mild Cognitive Impairment (MCI).

Forty-six patients with MCI were randomly divided into two groups; (a) the training group, which received a computer-based multidomain cognitive training program with the use of the RehaCom software and (b) the control group, which underwent standard-clinical care. The duration of the computer-based training program was 15 weeks, administered twice a week for approximately one hour per session.

Analysis of the baseline versus endpoint performance of each group demonstrated that in the control group delayed memory and executive function had deteriorated over the observation period of 15 weeks,

while improvement was observed in the training group's performance on delayed memory, word recognition, Boston Naming Test (BNT), Clock Drawing Test (CDT), Semantic Fluency (SF), Trail Making Test-A (TMT-A) and Trail Making Test-B (TMT-B).

Comparison between the two groups presented a significant effect of the intervention for most cognitive domains. These findings are promising for the development of training methods designed to delay cognitive decline in patients with MCI, which is considered to be the prodromal stage of Alzheimer's Disease (AD).

# Beneficial Effect of Multidomain Cognitive Training on the Neuropsychological Performance of Patients with Early-Stage Alzheimer's Disease



Nousia A, Siokas V, Aretouli E, Messinis L, Aloizou AM, Martzoukou M, Karala M, Koumpoulis C, Nasios G, Dardiotis E  
Hindawi, *Neural Plasticity*, Volume 2018, Article ID 2845176, <https://doi.org/10.1155/2018/2845176>

**BACKGROUND AND PURPOSE:** There is an increasing interest in the effect of nonpharmacological interventions on the course of patients with Alzheimer's disease (AD). The objective of the present study is to determine the benefits of a structured, multidomain, mostly computer-based, cognitive training (MCT) on the cognitive performance of patients with early-stage AD.

**METHOD:** Fifty patients with early-stage AD participated in the study. Patients were randomly allocated either to the training program group () or to a wait list control group (). The training program group received computer-assisted MCT and linguistic exercises utilizing pen and paper supplemented by cognitive-linguistic exercises for homework. The duration of the MCT intervention program was 15 weeks, and it was administered twice a week. Each session lasted for approximately one hour. Objective measures of episodic memory, delayed memory, word recognition, attention, executive function, processing speed, semantic fluency, and naming were assessed at baseline and after the completion of the program in both groups.

**RESULTS:** Analysis showed that in controls, delayed memory and executive function had deteriorated over the observation period of 15 weeks, while the training group improved their performance in word recognition, Boston Naming Test (BNT), semantic fluency (SF), clock-drawing test (CDT), digit span forward (DSF), digit span backward (DSB), trail-making test A (TMT A), and trail-making test B (TMT B). Comparison between the training group and the controls showed that MCT had a significant beneficial effect in delayed memory, naming, semantic fluency, visuospatial ability, executive functions, attention, and processing speed.

**CONCLUSIONS:** The study provides evidence of a beneficial effect of MCT with an emphasis on cognitive-language performance of patients with early-stage AD. Considering the limited efficacy of current pharmacological therapies in AD, concurrent computer-based MCT may represent an additional enhancing treatment option in early-stage AD patients.

# Computerized Cognitive Training in Older Adults With Mild Cognitive Impairment or Dementia: A Systematic Review and Meta-Analysis



Hill NT, Mowszowski L, Naismith SL, Chadwick VL, Valenzuela M, Lampit A  
The American journal of psychiatry 2017 Apr 1;174(4):329-340. doi: 10.1176/appi.ajp.2016.16030360

**OBJECTIVE:** Previous meta-analyses indicate that computerized cognitive training (CCT) is a safe and efficacious intervention for cognition in older adults. However, efficacy varies across populations and cognitive domains, and little is known about the efficacy of CCT in people with mild cognitive impairment or dementia.

**METHOD:** The authors searched Medline, Embase, PsychINFO, CINAHL, and CENTRAL through July 1, 2016, for randomized controlled trials of CCT in older adults with mild cognitive impairment or dementia. Overall cognition, individual cognitive domains, psychosocial function, and activities of daily living were pooled separately for mild cognitive impairment and dementia trials.

**RESULTS:** The overall effect on cognition in mild cognitive impairment across 17 trials was moderate (Hedges'  $g=0.35$ , 95% CI=0.20–0.51). There was

no evidence of publication bias or difference between active- and passive-controlled trials. Small to moderate effects were found for global cognition, attention, working memory, learning, and memory, with the exception of nonverbal memory, and for psychosocial functioning, including depressive symptoms. In dementia, statistically significant effects were found on overall cognition ( $k=11$ ,  $g=0.26$ , 95% CI=0.01–0.52) and visuospatial skills, but these were driven by three trials of virtual reality or Nintendo Wii.

**CONCLUSIONS:** CCT is efficacious on global cognition, select cognitive domains, and psychosocial functioning in people with mild cognitive impairment. This intervention therefore warrants longer-term and larger-scale trials to examine effects on conversion to dementia. Conversely, evidence for efficacy in people with dementia is weak and limited to trials of immersive technologies.

## The Effects of Cognitive Rehabilitation Training on Cognitive Function of Elderly Dementia Patients



Oh BH, Kim YK, Kim JH, Shin YS  
J Korean Neuropsychiatr. Assoc. 2003, Vol 42, No 4, 514-519

**OBJECTIVES:** This study was to evaluate the effects of cognitive rehabilitation training on the cognitive decline of elderly dementia patients.

**METHODS:** Each of 20 subjects received 16 sessions of repeated training with computer-aided cognitive rehabilitation program (REHACOM). Cognitive function of all subjects were evaluated by K-DRS, K-BNT, K-MMSE and GDS before and after the training.

**RESULTS:** Significant improvement of attention and memory was observed following REHACOM. There was no significant change in visuospatial memory, executive function, and conceptualization.

**CONCLUSION:** It is suggested that cognitive rehabilitation training with elderly dementia patients can be useful to ameliorate the cognitive decline and to enhance motivation and self-esteem.

# WOME: Theory-Based Working Memory Training - A Placebo-Controlled, Double-Blind Evaluation in Older Adults



frontiers  
in Aging Neuroscience

Weicker J, Hudl N, Frisch S, Lepsien J, Mueller K, Villringer A, Thöne-Otto A

Front Aging Neurosci. 2018 Aug 14;10:247. doi: 10.3389/fnagi.2018.00247. eCollection 2018

**BACKGROUND:** Scientifically evaluated cognitive intervention programs are essential to meet the demands of our increasingly aging society. Currently, one of the „hottest“ topics in the field is the improvement of working memory function and its potential impact on overall cognition. The present study evaluated the efficacy of WOME (WORKing MEMory), a theory-based working memory training program, in a double-blind, placebo-controlled, and randomized controlled trial ([www.drks.de](http://www.drks.de), DRKS00013162).

**METHODS:** N = 60 healthy older adults were allocated to (1) the WOME intervention, (2) an active low-level intervention, or (3) a passive control group. Overall, the intervention groups practiced twelve sessions of 45 min within 4 weeks of their respective training. Transfer effects were measured via an extensive battery of neuropsychological tests and

questionnaires both pre-/post-training and at a 3-month follow-up.

**RESULTS:** WOME led to a significant improvement in working memory function, demonstrated on a non-trained near transfer task and on two different composite scores with moderate to large effect sizes. In addition, we found some indication of relevant impact on everyday life. The effects were short-term rather than stable, being substantially diminished at follow-up with only little evidence suggesting long-term maintenance. No transfer effects on other cognitive functions were observed.

**CONCLUSION:** WOME is an appropriate and efficient intervention specifically targeting the working memory system in healthy older adults.

## Memory enhancement in healthy older adults using a brain plasticity-based training program: a randomized, controlled study



Mahncke HW, Connor BB, Appelman J, Ahsanuddin ON, Hardy JL, Wood RA, Joyce NM, Boniske T, Atkins SM, Merzenich MM. Proc Natl Acad Sci U S A. 2006 Aug 15;103(33):12523-8. Epub 2006 Aug 3.

Normal aging is associated with progressive functional losses in perception, cognition, and memory. Although the root causes of age-related cognitive decline are incompletely understood, psychophysical and neuropsychological evidence suggests that a significant contribution stems from poorer signal-to-noise conditions and down-regulated neuromodulatory system function in older brains. Because the brain retains a lifelong capacity for plasticity and adaptive reorganization, dimensions of negative reorganization should be at least partially reversible through the use of an appropriately designed training program. We report here results from such a training program targeting age-related cognitive decline. Data from a randomized, controlled trial

using standardized measures of neuropsychological function as outcomes are presented. Significant improvements in assessments directly related to the training tasks and significant generalization of improvements to nonrelated standardized neuropsychological measures of memory (effect size of 0.25) were documented in the group using the training program. Memory enhancement appeared to be sustained after a 3-month no-contact follow-up period. Matched active control and no-contact control groups showed no significant change in memory function after training or at the 3-month follow-up. This study demonstrates that intensive, plasticity-engaging training can result in an enhancement of cognitive function in normal mature adults.



## Effects of Computer-assisted Cognitive Rehabilitation Training on the Cognition and Static Balance of the Elderly.



Lee YM, Jang C, Bak IH, Yoon JS (2013).

Journal of Physical Therapy Science 25(11):1475-7

**PURPOSE:** The purpose of this study was to investigate the effects of a six-week-long computer-assisted cognitive rehabilitation training program on the improvement of cognition and balance abilities of the elderly.

**SUBJECTS:** Thirty healthy elderly people, aged 65 to 80, were randomly assigned either to the training group (n=15) or the control group (n=15).

**METHODS:** Cognitive functions were evaluated using MMSE-K, and the BioRescue AP 153 (RMINGENIERIE, France) was used to examine subjects' changes in static balance.

**RESULTS:** The MMSE-K score showed a significant change over the course of the treatment period in the training group, but not in the control group. The sway area and sway path length decreased significantly in the training group, but it did not show any changes in the control group.

**CONCLUSION:** Computer-assisted cognitive rehabilitation training is an effective intervention method for the improvement of the cognition and balance abilities of the elderly.

# Attention-deficit hyperactivity disorder (ADHD)

## Evaluation of a computer-based neuropsychological Training in Children with Attention-Deficit Hyperactivity Disorder (ADHD)

NeuroRehabilitation

Amonn F, Frölich J, Breuer D, Banaschewski T, Doepfner M  
NeuroRehabilitation. 2013;32(3):555-62. doi: 10.3233/NRE-130877

**BACKGROUND:** We report the effects of a computer-based neuropsychological training in children with Attention-Deficit Hyperactivity Disorder (ADHD). We hypothesized that a specific training focusing on attentional dysfunction would result in an improvement of inattention, observable in test performance, behavior and performance during experimental school lessons and in parent and teacher ratings of the related core symptom.

**METHOD:** We chose a within-subject-control-design with a 4 week baseline period and subsequent 12 to 15 weekly training-sessions. 30 children (6 to 13 years old) with a diagnosis of ADHD (ICD 10: F 90.0) and no other comorbidities participated in the study.

**RESULTS:** The training revealed significant improvement in training parameters of the neuropsychological training and in the symptoms of inattention and department as rated during experimental school lessons. However, generalization of training effects as measured by parent and teacher ratings was not detected.

**CONCLUSIONS:** We conclude that neuropsychological training could be helpful as one adjunct module in the complex treatment of ADHD but to prove clinical value, similar training programs must focus more strongly on individually existing neuropsychological deficits. Training programs should be more intensive and should eventually be combined with home based training access.

## The efficacy of computer-based cognitive training for executive dysfunction in schizophrenia

Psychiatry Research  
Neuroimaging

Mak M, Tyburski E, Starkowska A, Karabanowicz E, Samochowiec A, Samochowiec J  
Psychiatry Res. 2019 Jul 1;279:62-70. doi: 10.1016/j.psychres.2019.06.041

The purpose of this study was to assess the effect of computer-based cognitive training on executive dysfunction in patients with schizophrenia. Sixty-five patients with schizophrenia were randomly assigned to a training group (n=33) or a non-training group (n=32), and compared in terms of executive performance to a healthy control group (n=33). Executive function was assessed using the Trail Making Test, the Stroop Color and Word Test, and the Wisconsin Card Sorting Test (computer version). Cognitive training was performed using RehaCom software over a course of 16 individual sessions. Primary outcomes were training (performance at

three different timepoints) and neuropsychological components (flexibility and cognitive inhibition, high executive processing, and processing speed). In both clinical groups, all aspects of executive function were found to be deficient. In the patient training group, the use of computer-based training alongside pharmacological treatment was more effective in terms of cognitive improvement than pharmacological treatment alone. However, there was no significant effect of cognitive training on processing speed. Cognitive training in schizophrenia patients was effective at improving several aspects of executive function, but did not improve processing speed.

## The implementation of cognitive remediation interventions in Campania

Journal of  
PSYCHOPATHOLOGY

Palumbo D, Patriarca S, Mucci A, De Angelis M, Di Crosta I, Piegari G, Galderisi S  
JOURNAL OF PSYCHOPATHOLOGY, 2018; 24:98-103

Cognitive impairment is considered a core aspect of schizophrenia and an important therapeutic target for its negative impact on real-life functioning of affected people. Psychotropic drugs commonly used in the treatment of schizophrenia do not improve and might even worsen cognitive dysfunctions. In contrast, cognitive remediation (CR) was found to improve cognitive deficits and real-life functioning of subjects with schizophrenia. The present paper aims to provide a brief review of the theoretical basis of different CR programs and to illustrate the

implementation of two such programs in Campania. In particular, the Social Skills And Neurocognitive Individualized Training (SSANIT) and the Computerized Interactive Remediation of Cognition - Training for Schizophrenia (CIRCuiTS) will be illustrated. SSANIT is an integrated program, including individualized computerized CR and social skills trainings. CIRCuiTS is a stand-alone computerized CR program targeting the development of metacognitive skills. Factors informing the choice of a specific CR program for individual subjects are also illustrated.

# Preliminary study of a rehabilitation program based on attentional processes to treat auditory hallucinations



López-Luengo B, Muela-Martínez JA

Cogn Neuropsychiatry. 2016 Jul;21(4):315-334. Epub 2016 Jul 18.

**INTRODUCTION:** Despite the effectiveness of pharmacological treatment, residual hallucinations do not completely resolve in some medicated patients. The aim of this study was to investigate the efficacy of attention training for reducing hallucinations in individuals with psychosis.

**METHODS:** A randomized controlled trial was performed in which 20 individuals suffering auditory hallucinations received auditory stimulation similar to their internal voices, which was integrated into the RehaCom program of attention training. An equal number of individuals suffering auditory hallucinations did not receive this training. Cognitive and symptomatological variables were evaluated before and after the intervention period in both groups.

**RESULTS:** Only data of 16 subjects were analyzed. Auditory hallucinations no longer occurred by the end of the training program in five of eight individuals, whereas their frequency, intensity and negative content and associated anxiety were significantly reduced in the remaining three. No changes in hallucinations were observed in the control group. Attentional processes and executive functions were significantly better in patients who underwent the training than in those who did not at the end of the intervention period.

**CONCLUSIONS:** Attention training can help people with auditory hallucinations develop an ability to ignore them, which can reduce or eliminate them entirely.

## The effectiveness of computerized cognitive rehabilitation training program in improving cognitive abilities of schizophrenia clients



Mohammadi MR, Keshavarzi Z, Talepasand S

Iran J Psychiatry. 2014 Oct;9(4):209-15.

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

**METHOD:** A total of 15 clinically stable out patients with Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) criteria for schizophrenia, diagnosed with different types of schizophrenia: paranoid, disorganized, residual, based on DSM-IV-TR were selected to participate in this study. All patients were randomly selected using a conventional sampling method and assigned to 60 hours individual sessions of computer - assisted cognitive

remediation (CACR). This was a pre-experimental study with pretest and posttest in a single group. Cognitive functions were checked with Continuous Performance Test (CPT), Wechsler Adult Intelligence Scale (Wds) and Prospective and Retrospective Memory Questionnaire (PRMQ). The symptoms of patients were measured with the Positive and Negative Syndrome Scale (PANSS). Remediation was performed utilizing the RehaCom® software. Patients received the cognitive remediation program including attention, concentration and working memory. All participants were followed up after an interval of one month and three months. Data were analyzed using repeated measures analysis.

Acquired Brain Injury  
Neurodegenerative Diseases  
Prevention of cognitive Deterioration / Geriatrics  
Neurodevelopmental Disorders  
Mental Illness  
Combination Therapy

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

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

## Neurocognitive individualized training versus social skills individualized training: a randomized trial in patients with schizophrenia.

**SCHIZOPHRENIA RESEARCH**  
The Official Journal of the Schizophrenia International Research Society

Bucci, P., Piegari, G., Mucci, A., Merlotti, E., Chieffi, M., De Riso, F., ... & Galderisi, S. (2013). Schizophrenia research, 150(1), 69-75.

Rehabilitation programs integrating cognitive remediation (CR) and psychosocial rehabilitation are often implemented as they seem to yield greater improvements in functional outcome than stand-alone treatment approaches. Mechanisms underlying synergistic effects of combining CR with psychosocial interventions are not fully understood. Disentangling the relative contribution of each component of integrated programs might improve understanding of underlying mechanisms. In the present study we compared the efficacy of two components of our rehabilitation program [the Neurocognitive Individualized Training (NIT) and the Social Skills Individualized Training (SSIT)].

Seventy-two patients with schizophrenia or schizoaffective disorder were randomly assigned to one of two treatment groups. Changes in cognitive, psychopathological and real-world functioning indices after

6 and 12 months were compared between the two groups. After both 6 and 12 months, NIT produced an improvement of attention, verbal memory and perseverative aspects of executive functioning, while SSIT produced a worsening of visuo-spatial memory and attention and no significant effect on the other cognitive domains. As to the real-world functioning, NIT produced a significant improvement of interpersonal relationships, while SSIT yielded a significant improvement of QLS instrumental role subscale.

According to our findings, cognitive training is more effective than social skills training on several cognitive domains and indices of real-world functioning relevant to subject's relationships with other people. Integrated approaches might target different areas of functional impairment but should be planned carefully and individually to fully exploit the synergistic potential.

## The efficacy of cognitive neurorehabilitation with RehaCom program in schizophrenia patients

**Psychiatria Polska**

Mak M, Tybura P, Bieńkowski P, Karakiewicz B, Samochowiec J. Psychiatr Pol. 2013 Mar-Apr;47(2):213-23

Schizophrenic patients present cognitive dysfunctions which are currently regarded to be one of endophenotypic markers predisposing to schizophrenia. This indicates neuro-structural changes underlying schizophrenia, which can be treated as a neuro-degenerative and neuro-developing disease.

**AIM:** The purpose of this study was to assess the possibility of neuropsychological rehabilitation in schizophrenia.

**METHODS:** 41 participants and 40 control subjects were randomly selected and did not show differences

Acquired  
Brain Injury

Neurodegenerative  
Diseases

Prevention of cognitive  
Deterioration / Geriatrics

Neurodevelopmental  
Disorders

Mental  
Illness

Combination  
Therapy

in gender, age and illness duration. Both groups had the diagnosis of paranoid schizophrenia according to ICD-10 criteria and were treated with antipsychotic drugs. Cognitive functions were checked with Wisconsin Card Sorting Test (WCST), Trail Making Test (TMT), and Stroop Color -Word Interference Test (SCWT) in the beginning and in the end of the experiment. In the research group each patient was trained with the rehabilitation programs that focused on attention and concentration and topological memory. This group was compared with the control group that was not trained with RehaCom.

**RESULTS:** RehaCom procedures apparently can be useful in neuropsychological rehabilitation of cognitive dysfunctions in patients with diagnosed

schizophrenia. Every participant from the research group showed a significant improvement in the training programs, especially in attention/concentration procedure. The analysis of parameters obtained in the neuropsychological tests showed some improvement in neuropsychological assessment in both groups.

**CONCLUSIONS:** Cognitive rehabilitation produces moderate improvement in cognitive functioning. A comprehensive treatment using also new technologies supporting pharmacological treatments and other therapies should result in increased cognitive functioning and as a consequence improvement of quality of patient's life.

## How can cognitive remediation therapy modulate brain activations in schizophrenia? An fMRI study



Bor J, Brunelin J, d'Amato T, Costes N, Suaud-Chagny M, Saoud M, Poulet E  
 June 30, 2011 Volume 192, Issue 3, Pages 160-166

Cognitive remediation therapy (CRT) is a non-biological treatment that aims to correct cognitive deficits through repeated exercises. Its efficacy in patients with schizophrenia is well recognized, but little is known about its effect on cerebral activity. Our aim was to explore the impact of CRT on cerebral activation using functional magnetic resonance imaging (fMRI) in patients with schizophrenia. Seventeen patients and 15 healthy volunteers were recruited. Patients were divided into two groups: one group received CRT with RehaCom® software (n=8), while a control group of patients (non-CRT group) received no additional treatment (n=9). The three groups underwent two fMRI sessions with an

interval of 3 months: they had to perform a verbal and a spatial n-back task at the same performance level. Patients were additionally clinically and cognitively assessed before and after the study. After CRT, the CRT group exhibited brain over-activations in the left inferior/middle frontal gyrus, cingulate gyrus and inferior parietal lobule for the spatial task. Similar but nonsignificant over-activations were observed in the same brain regions for the verbal task. Moreover, CRT patients significantly improved their behavioral performance in attention and reasoning capacities. We conclude that CRT leads to measurable physiological adaptation associated with improved cognitive ability.

## A randomized, controlled trial of computer-assisted cognitive remediation for schizophrenia



d'Amato T, Bation R, Cochet A, Jalenques I, Galland F, Giraud-Baro E, Pacaud-Troncin M, Augier-Astolfi F, Llorca PM, Saoud M, Brunelin J.; Schizophr Res. 2011 Feb; 125(2-3):284-90. doi: 10.1016/j.schres.2010.10.023. Epub 2010 Nov 19.

**OBJECTIVE:** There is considerable interest in cognitive remediation for schizophrenia. Our study aimed to evaluate, in a large sample of patients with schizophrenia, the interest of a computer-assisted

cognitive remediation program on cognitive performances of patients as well as in clinical and functional outcome.

**METHOD:** Seventy-seven patients with remitted schizophrenia were randomly assigned to 14 2-hours individual sessions of computer-assisted cognitive remediation (n=39) or a control condition (n=38). Remediation was performed using RehaCom® software. Four procedures were chosen to train four cognitive functions involved in different stages of the information processing: attention/concentration, working memory, logic, and executive functions. Primary outcomes were remediation exercise metrics, neuropsychological composites (episodic memory, working memory, attention, executive functioning, and processing speed), clinical and community functioning measures.

**RESULTS:** Cognitive performances concerning attention/vigilance, verbal working memory and verbal learning memory and reasoning/problem solving improved significantly in the remediation condition when no difference was reported in the control condition between the 2 assessments. However, there were no significant benefits of cognitive remediation on non-verbal working memory and learning and speed of processing or functional outcome measures.

**CONCLUSIONS:** Cognitive remediation for people with schizophrenia was effective in improving performance, but the benefits of training did not generalize to functional outcome measures. Long term follow-up studies are needed to confirm the maintenance of such improvements.

## Impact of a new cognitive remediation strategy on interpersonal problem solving skills and social autonomy in schizophrenia].



Cochet A, Saoud M, Gabriele S, Broallier V, El Asmar C, Daléry J, D'Amato T. *Encephale*. 2006 Mar-Apr;32(2 Pt 1):189-95. French. doi: 10.1016/s0013-7006(06)76144-9. PMID: 16910619

**INTRODUCTION:** Despite recent developments, the impact of pharmacotherapy on social autonomy and interpersonal problem solving skills in patients with schizophrenia remains limited, with consequences in terms of socio-professional functioning. Indeed, independently of the positive, negative and/or disorganization symptoms, functional deficits in patients with schizophrenia rely mainly on various cognitive impairments.

**OBJECTIVES:** To determine the impact of a new Cognitive Remediation Strategy on interpersonal problem solving skills, social autonomy and symptoms in patients with schizophrenia.

**METHODS:** Thirty patients with schizophrenia were enrolled in a program consisting of 14 training sessions of 4 cognitive functions (attention/concentration, topological memory, logical reasoning, executive functions) using the RehaCom software. Measurements of attention (Continuous Performance Test,

CPT), memory (Rivermead Behavioural Memory Test, RBMT) and executive functions (Wisconsin Card Sorting Test, WCST) as well as interpersonal problem solving skills (Assessment of Interpersonal Problem-Solving Skills, AIPSS) and social autonomy (Social Autonomy Scale, EAS) and finally schizophrenia symptoms (Positive And Negative Syndrome Scale, PANSS) were undertaken at the beginning and the end of the 14 remediation meetings.

**RESULTS:** Cognitive functions, interpersonal problems solving skills, social autonomy and symptoms were significantly improved by the Cognitive Remediation Strategy.

**CONCLUSION:** Our results confirm the therapeutic impact of a Cognitive Remediation Strategy among 30 schizophrenic patients stabilized on clinical, therapeutic and functional levels. The question of the long-term maintenance of such improvements still requires further investigation.

## Online neurocognitive remediation therapy to improve cognition in community-living individuals with a history of depression: A pilot study.

EUROPEAN  
PSYCHIATRY

Semkovska, M., & Ahern, E. (2017).

Internet Interventions, 9, 7-14.

Major depression is a highly prevalent psychopathology with high relapse rates. Following remission from a depressive episode, neurocognitive difficulties in attention, working memory and executive function often persist, preventing full clinical recovery. These neurocognitive deficits are often present since the first depressive episode and have been shown to predict relapse.

The efficacy of computerised neurocognitive remediation therapy (NCRT) to improve attention, memory and executive function has been demonstrated in several clinical populations but randomised controlled trials (RCT) have not been conducted in depression.

The present study aimed to conduct a pilot, randomised study, of computerised NCRT for individuals with past depression, currently in remission. Twenty-two

individuals remitted from depression were randomly assigned to receive 20 one-hour sessions over 5 weeks of either computerised NCRT or a component-equivalent allocation (play online computer games).

The NCRT group showed significantly larger improvements in performance relative to the Games group in the three targeted neurocognitive domains: divided attention, verbal working memory, and planning, but also in non-targeted domains of long-term verbal memory and switching abilities. No significant effect was observed in the NCRT-targeted domain visual working memory. These preliminary results suggest computerised NCRT efficacy to improve targeted neurocognitive processes during depression remission and support its potential value as preventative connected intervention tool.



# Efficacy of Neurocognitive Remediation Therapy During an Acute Depressive Episode and Following Remission: Results From Two Randomised Pilot Studies

EUROPEAN  
PSYCHIATRY

Semkovska M, Ahern E, Lonergain D.O, Lambe S, McLaughlin D.M.

European Psychiatry, Volume 30, Supplement 1, 28–31 March 2015, Pages 403

**INTRODUCTION:** Major depression is the most prevalent psychiatric disorder with high relapse rates. Following usual treatment, mood may improve but neurocognitive difficulties often persist, preventing full return to normal social function. These deficits worsen with repeated depressive episodes and are a significant predictor of relapse. The efficacy of neurocognitive remediation therapy (NCRT) to rehabilitate cognition has been demonstrated in several neurological and psychiatric populations but randomized controlled trials (RCT) have not been conducted in depression.

**OBJEKTIVE:** Conduct two randomized controlled pilot studies to determine the feasibility and obtain preliminary efficacy data of NCRT in (1) acutely depressed, hospitalized patients; and (2) community-living remitters from recurrent depression.

**METHODS:** In Pilot 1, 24 inpatients hospitalized for major depression were randomized to computerized NCRT or playing computer games for five weeks with four one-hour individual sessions weekly. NCRT targeted divided attention, working

memory and planning. In Pilot 2, 20 community-living remitters from recurrent depression were randomized to the same intervention arms, but their administration was home-based from the program start. In both studies, before the intervention start and within a week of the final session, standardized assessments of cognition and depression severity were conducted.

**RESULTS:** The feasibility assessment demonstrated good recruitment and compliance rates, excellent acceptance of randomization. Preliminary outcome data showed improvement in 80% of the targeted cognitive domains following NCRT comparatively to the control condition.

**CONCLUSIONS:** These pilot studies support the feasibility and value of conducting an RCT of computerized NCRT for neurocognitive deficits in both acutely depressed and remitted individuals.

Acquired  
Brain Injury

Neurodegenerative  
Diseases

Prevention of cognitive  
Deterioration / Geriatrics

Neurodevelopmental  
Disorders

Mental  
Illness

Combination  
Therapy

### Enhancing cognitive training effects in Alzheimer's disease: rTMS as an add-on treatment.



Bagattini, C., Zanni, M., Barocco, F., Caffarra, P., Brignani, D., Miniussi, C., & Defanti, C. A. (2020). *Brain Stimulation*, 13(6), 1655-1664.

The treatment of Alzheimer's disease (AD) in the field of non-pharmacological interventions is a challenging issue, given the limited benefits of the available drugs. Cognitive training (CT) represents a commonly recommended strategy in AD. Recently, repetitive transcranial magnetic stimulation (rTMS) has gained increasing attention as a promising therapeutic tool for the treatment of AD, given its ability of enhancing neuroplasticity.

In the present randomized, double-blind, sham-controlled study, we aimed at investigating the add-on effect of a high frequency rTMS protocol applied over the left dorsolateral prefrontal cortex (DLPFC) combined with a face-name associative memory CT in the continuum of AD pathology. Fifty patients

from a very early to a moderate phase of dementia were randomly assigned to one of two groups: CT plus real rTMS or CT plus placebo rTMS.

The results showed that the improvement in the trained associative memory induced with rTMS was superior to that obtained with CT alone. Interestingly, the extent of the additional improvement was affected by disease severity and levels of education, with less impaired and more educated patients showing a greater benefit. When testing for generalization to non-trained cognitive functions, results indicated that patients in CT-real group showed also a greater improvement in visuospatial reasoning than those in the CT-sham group. Interestingly, this improvement persisted over 12 weeks after treatment beginning.

## Effect of transcranial direct current stimulation on cognitive function in stroke patients.



Shaker, H. A., Sawan, S. A. E., Fahmy, E. M., Ismail, R. S., & Abd Elrahman, S. A. E. (2018). The Egyptian journal of neurology, psychiatry and neurosurgery, 54(1), 1-8.

**BACKGROUND:** Cognitive impairment after stroke is common and can cause disability with major impacts on quality of life and independence. Transcranial direct current stimulation may represent a promising tool for reconstitution of cognitive functions in stroke patients.

**OBJECTIVES:** This study aimed to investigate the effect of transcranial direct current stimulation on cognitive functions in stroke patients.

**PATIENTS AND METHODS:** Forty male stroke patients were included. Patients were divided randomly into two equal groups (A and B). Group A received transcranial direct current stimulation (tDCS) in combination with selected cognitive training program by

RehaCom. Group B received sham transcranial direct current stimulation in combination with the same cognitive training program. Cognitive evaluation and functional independence measure (FIM) were done for all patients before and after treatment.

**RESULTS:** There was a significant improvement in the scores of attention and concentration, figural memory, logical reasoning, reaction behavior, and FIM post treatment in both groups; the improvement was significantly higher in group A compared to group B.

**CONCLUSION:** tDCS is a safe and effective neuro-rehabilitation modality that improves post stroke cognitive dysfunctions. Moreover, tDCS has a positive impact on performance of daily activities.

### Effects of virtual reality immersive training with computerized cognitive training on cognitive function and activities of daily living performance in patients with acute stage stroke: A preliminary randomized controlled trial.



Cho, D. R., & Lee, S. H. (2019).  
Medicine, 98(11).

**OBJECTIVE:** The purpose of this study was to investigate the impact of virtual reality immersive training with computerized cognitive training on the cognitive function and activity of daily living in patients with acute stroke.

**METHOD:** We included 42 patients with acute stage stroke from C hospital in Sungnam from May, 2017 to September, 2017. The patients were randomly selected and divided into the experimental (n = 21) and control (n = 21) group. The experimental group performed virtual reality training, including Head Mount Display with computerized cognitive therapy, and the control group performed computerized cognitive therapy. Both groups trained for 30 minutes a day 5 times a week; the intervention lasted

4 weeks. To evaluate the improvement in each group, pre-post-test evaluation was conducted using the Loewenstein Occupational Therapy Cognitive Assessment and Computerized Neurocognitive Function Test for cognitive function, and Functional Independent Measure for activities of daily living.

**RESULTS:** Attention and memory in cognitive function and activity of daily living performance were improved in both groups.

**CONCLUSION:** Virtual reality immersive training might be an affordable approach for cognitive function and activity of daily living performance recovery for patients with acute stroke.

Acquired Brain Injury  
Neurodegenerative Diseases  
Prevention of cognitive Deterioration / Geriatrics  
Neurodevelopmental Disorders  
Mental Illness  
Combination Therapy

## Effects of computerized cognitive training and tai chi on cognitive performance in older adults with traumatic brain injury.



Hwang, H. F., Chen, C. Y., Wei, L., Chen, S. J., Yu, W. Y., & Lin, M. R. (2020). The Journal of Head Trauma Rehabilitation, 35(3), 187-197.

**OBJECTIVE:** To compare the effects of computerized cognitive training (CCT) and tai chi (TC) with usual care (UC) on cognitive functions and secondary outcomes in older adults with traumatic brain injury.

**PARTICIPANTS AND SETTINGS:** Ninety-six patients aged 55 years and older who had a diagnosis of traumatic brain injury requiring hospital admission.

**DESIGN:** Randomized controlled trial. Main Measures: The Mattis Dementia Rating Scale (MDRS), Mini-Mental State Examination, modified Telephone Interview of Cognitive Status, and Trail Making Tests A and B.

**RESULTS:** Compared with UC, CCT increased scores on the MDRS's total, attention, and memory and those on the Mini-Mental State Examination and Telephone Interview of Cognitive Status over the

6-month intervention; TC increased scores on the MDRS's total and conceptualization and those on the Mini-Mental State Examination over the 6-month intervention, while it also increased scores on the MDRS's total and initiation/preservation and those on the Telephone Interview of Cognitive Status and reduced the time to complete the Trail Making Test B over the 12-month study. Furthermore, compared with UC, CCT increased handgrip strength and TC reduced the time to complete 5 sit-to-stands over the 6-month intervention.

**CONCLUSION:** Both CCT and TC may improve global cognition and different specific cognitive domains in older traumatic brain injury patients; the TC's effect may last for at least an additional 6 months.

Acquired  
Brain Injury

Neurodegenerative  
Diseases

Prevention of cognitive  
Deterioration / Geriatrics

Neurodevelopmental  
Disorders

Mental  
Illness

Combination  
Therapy

# Clinical Efficacy of Acupuncture Treatment in Combination With RehaCom Cognitive Training for Improving Cognitive Function in Stroke: A 2 x 2 Factorial Design Randomized Controlled Trial



Jiang C, Yang S, Tao J, Huang J, Li Y, Ye H, Chen S, Hong W, Chen L;

J Am Med Dir Assoc. 2016 Aug 31. pii: S1525-8610(16)30299-7. doi: 10.1016/j.jamda.2016.07.021. Epub 2016 Aug 31

**OBJECTIVE:** The aim of this study was to identify the clinical efficacy of acupuncture in combination with RehaCom cognitive training in post-stroke patients with cognitive dysfunction.

**METHODS/DESIGN:** This study was a 2 x 2 factorial design randomized controlled trial comparing acupuncture, computer-assisted cognitive rehabilitation, and the usual treatment by per-protocol analysis. The trial was completed by 204 stroke patients, including 49 patients in a control group, 52 patients in an acupuncture treatment group, 51 patients in a RehaCom training group, and 52 patients in an acupuncture combined with RehaCom group. All of the patients accepted basic treatment and health education. The interventions continued for 12 weeks (30 minutes per day, 5 days per week). The relative cognitive and functional outcomes were measured at baseline and 12 weeks (at the end of intervention) using the Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), and Functional Independence Measure (FIM) scales.

**RESULTS:** After 12 weeks of treatment, the functional statuses of the patients in each of the 4 groups showed varying degrees of improvement. Multiple comparisons of the changes in the MMSE, MoCA, and FIM scores indicated that acupuncture combined with RehaCom cognitive training (ACR) had enhanced therapeutic effects on the functional statuses of the stroke patients ( $P < .05$ ). In addition, ACR had similar therapeutic effects on the functional statuses of the stroke patients according to each of the assessment scales applied ( $P\Delta$  change value MMSE = 0.399,  $P\Delta$ MoCA = 0.794,  $P\Delta$ FIM = 0.862). The interaction effect values between acupuncture and RehaCom training (acceptance or non-acceptance) were as follows:  $\Delta$ MMSE:  $F = 6.251$ ,  $P = .013$ ;  $\Delta$ MoCA:  $F = 4.991$ ,  $P = .027$ ; and  $\Delta$ FIM:  $F = 6.317$ ,  $P = .013$ . Further, the main effect values for acupuncture and RehaCom training were both significant ( $P < .05$ ).

**CONCLUSIONS:** There is an interaction effect in the treatment of stroke patients using ACR. The use of acupuncture in combination with RehaCom training has better therapeutic effects on the functional statuses of post-stroke patients than the use of either treatment alone, demonstrating the clinical significance of this combination therapy.



