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# Studies and Meta-Analysis

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# 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 neuro-psychological 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)

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



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.

## 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.

## Effects of neurofeedback and computer-assisted cognitive rehabilitation on relative brain wave ratios and activities of daily living of stroke patients: a randomized control trial



Cho HY, Kim KT, Jung JH

J Phys Ther Sci. 2016 Jul; 28(7): 2154-2158. Published online 2016 Jul 29. doi: 10.1589/jpts.28.2154

**PURPOSE:** This study investigated the effects of neurofeedback (NFB) and computer-assisted cognitive rehabilitation (CACR) on the relative brain wave ratios and activities of daily living (ADL) of stroke patients.

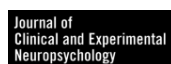
**SUBJECTS AND METHODS:** Forty-four participants were randomly allocated to the NFB ( $n=14$ ), CACR ( $n=14$ ), or control (CON) ( $n=16$ ) groups. Two expert therapists provided the NFB, CACR, and CON groups with traditional rehabilitation therapy in 30-minute sessions, 5 times a week, for 6 weeks. NFB training was provided only to the NFB group and CACR training was provided only to the CACR group. The CON group received traditional rehabilitation therapy only.

Before and after 6 weeks of intervention, brain wave and ADL evaluations were performed, and the results were analyzed.

**RESULTS:** The relative ratio of beta waves, only showed a significant increase in the frontal and parietal areas of the NFB group. Significant changes in ADL were shown by all three groups after the intervention. However, there were no significant differences between the NFB and CACR groups and the CON group.

**CONCLUSIONS:** Our results suggest that CACR and NFB are effective at improving cognitive function and ADL of stroke patients.

## Recovery after brain damage: Is there any indication for generalization between different cognitive functions?



Richter KM, Mödden C, Hanken K, Hildebrandt H

Clin Exp Neuropsychol. 2015; 37(6):571-80. doi: 10.1080/13803395.2015.1030358. Epub 2015 Jun 10.

**INTRODUCTION:** The question whether recovery in various cognitive functions is supported by one or two more fundamental functions (for instance, attentional or working memory functions) is a long-standing problem of cognitive rehabilitation. One possibility

to answer this question is to analyze the recovery pattern in different cognitive domains and to see whether improvement in one domain is related to performance in another domain.

**METHOD:** Ninety-two inpatients with stroke or other brain lesions (Barthel Index >75) were included. Neuropsychological assessment was done at the beginning and the end of a rehabilitation stay. Cognitive performance was analyzed at test and at domain level using conceptually and statistically defined composite scores for attention, immediate and delayed memory, working memory, prospective memory, and word fluency. We used regression analysis to look for generalization between cognitive domains.

**RESULTS:** Effect sizes of improvement varied largely (from  $d = 0.18$  in attention and  $d = 1.36$  in episodic

memory). Age, gender, and time since injury had no impact on recovery. Impaired patients showed significantly more improvement than non-impaired patients. Regression analysis revealed no effect of initial performance in one cognitive domain on improvements in other cognitive domains.

**CONCLUSION:** Significant recovery in impaired cognitive domains can be expected during neuropsychological rehabilitation. It depends more or less exclusively on improvement in the specific functions itself, and there was no evidence for generalization between cognitive domains.

## 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

# 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.

## The effectiveness of computer-assisted cognitive rehabilitation in brain-damaged patients

Polish  
Psychological  
Bulletin

Łojek E, Bolewska A

Polish Psychological Bulletin 2013, vol. 44(1), 31-39 DOI -10.2478/ppb-2013-0004

This study examined the effects of computer-assisted cognitive rehabilitation in a group of 16 brain-damaged patients. Therapeutic effectiveness was assessed by improvement on computer tasks, the results of neuropsychological tests and quality of life ratings. Participants suffered from mild to moderate attention and memory problems or aphasia. The procedure involved baseline assessment (pretest), a 15-week course of therapy conducted twice a week (30 hours in total) and posttest. Neuropsychological tests assessing attention, memory and language problems and quality of life ratings were administered twice: in pre- and posttests. Twelve healthy controls were also examined twice (with a 15-week interval) using the same battery of neuropsychological tests.

The RehaCom program and the Polish computer therapy program for aphasics called Afa-System were used for rehabilitation. The computer-assisted rehabilitation tasks were selected individually for each patient. The results showed significant improvement on computer-assisted tasks in all brain-damaged subjects. However, none or very little improvement was observed on neuropsychological tests and quality of life ratings. The results of the study confirm the importance of using different types of measures to estimate the effectiveness of computer-assisted neuropsychological rehabilitation as well as the necessity of applying various kinds of therapy to improve cognitive, emotional and social functioning in brain-damaged patients.



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



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



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.

# Is the Neuropsychological Treatment of Memory Specific or Unspecific? – Comparing Treatment Effects on Memory and Attention



Spahn V, Kulke H, Kunz M, Thöne-Otto A, Schupp W, Lautenbacher S;

Zeitschrift für Neuropsychologie : ZNP ; zugleich Organ der GNP; mit Mitteilungen der DGNKN. - 21 (2010), 4, 239 – 245

## PRIMARY OBJECTIVE AND RESEARCH DESIGN:

In order to analyze whether neuropsychological memory therapy acts specifically on the memory domain or in a more generalized fashion on further cognitive domains, 27 patients with organic memory deficits due to different etiologies (cerebrovascular, traumatic, infectious, etc.) were randomly assigned to two different memory treatment programs and investigated for changes in memory and attention.

**METHODS AND PROCEDURES:** Patients treated by a specific computer-based training of story recall (Training of Verbal Memory, TVM) were compared to a group in which compensational strategies for everyday memory problems were trained (Memory Therapy in Groups, MTG). Both therapies were

conducted over 12 to 15 sessions, 4-5 times per week, in addition to standard program of neuro-rehabilitation. Training effects were conducted over 12 to 15 sessions, 4-5 times per week, in addition to standard program of neurorehabilitation. Training effects were assessed for verbal and figural memory (Verbal Learning Test, Nonverbal Learning Test) and for attention (Alertness and Divided Attention in Test Battery of Attentional Performance).

**RESULTS AND CONCLUSIONS:** Both treatment groups resulted in improvement in tests of memory but not attention. This finding provides good evidence for the assumption of specificity of effects in neuropsychological treatment of memory.

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



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.

# 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.

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

Metaanalysis

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 consensual, 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.

# 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.

## New aspects of symptomatic MS treatment: Part 6 – cognitive dysfunction and rehabilitation

**Der Nervenarzt**

Henze T, Feneberg W, Flachenecker P, Seidel D, Albrecht H, Starck M, Meuth SG  
Der Nervenarzt, April 2018, Volume 89, Issue 4, pp 453–459

The symptomatic treatment of multiple sclerosis (MS) is nowadays of similar importance as immunotherapy within a comprehensive treatment concept of this chronic disease. It makes a considerable contribution to the reduction of disabilities in activities of daily living as well as social and occupational life. Moreover, symptomatic treatment is of great importance for amelioration of the quality of life. Since our last survey of symptomatic MS treatment in 2004 and publication of the guidelines of the German Neurological Society and the Clinical Competence

Network Multiple Sclerosis (“Klinisches Kompetenznetz Multiple Sklerose”, KKN-MS) in 2014 several developments within the topics of mobility, bladder and sexual function, vision, fatigue, cognition and rehabilitation have taken place. These new findings together with further aspects of disease measurement methods and overall treatment strategies of the respective symptoms, as well as treatment goals are introduced in several individual contributions. In this article the symptoms of cognitive disorders and the growing impact of rehabilitation are discussed.

## 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.

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



in Behavioral Neuroscience

Mattioli F, Bellomi F, Stampatori C, Provinciali L, Compagnucci L, Uccelli A, Pardini M, Santuccio G, Fre-

gonese 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.

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



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.

## 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.

## 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.

# 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", 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



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 (SCRCP) and another received a non-specific 8-week CR programme (NCRP) 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 SCRCP improved on 7 memory outcome measures, compared to only 1 in the NCRP 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.

## 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<sup>2</sup> 5.0%) 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.

## 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.

**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.

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



Mak M, Tybura P, Bieñkowski 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 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

Psychiatry Research  
Neuroimaging

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

SCHIZOPHRENIA  
RESEARCH  
The Official Journal of the Schizophrenia International Research Society

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.

## 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.

## 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 deportment 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 cognitive training programs in children and adolescents: a meta-analysis

Metaanalysis



Karch D, Albers L, Renner G, Lichtenauer N, von Kries R

Dtsch Arztebl Int. 2013 Sep;110(39):643-52. doi: 10.3238/arztebl.2013.0643. Epub 2013 Sep 27.

**BACKGROUND:** Cognitive therapies are intended to improve basic cognitive functions, whatever the cause of the deficiency may be. Children and adolescents with various cognitive deficits are treated with behavioral therapeutic and computer-supported training programs. We here report the first meta-analysis of the efficacy of such programs.

**METHODS:** We systematically searched the Medline, Embase, PsycINFO, PSYINDEX, and ERIC databases to find pertinent publications for a meta-analysis of cognitive training programs that are used in children and adolescents to improve attention, memory, and executive performance (primary goals) as well as behavior/psychopathology, intelligence, and school performance (secondary goals). The mean differences between the treatment and control groups are given here as standard deviation (SD) scores.

**RESULTS:** 1661 potentially relevant publications were found, including 22 studies that were considered in the meta-analysis, 17 of which were randomized controlled trials. The target variables were measured with more than 90 different testing techniques. The overall effects of cognitive training on attention (SD 0.18, 95% CI -0.11-0.47) and executive function (SD 0.17, 95% CI -0.12-0.46) were consistently small. A relatively strong effect was found on memory performance (0.65 SD, 95% [-0.12-1.42]), albeit with marked heterogeneity ( $I^2 = 82\%$ ) owing to two studies. The largest effect was found in the area of behavior and psychopathology (SD 0.58, 95% CI 0.31-0.85), but this last figure is derived mainly from studies that lacked an active control group.

**CONCLUSION:** Cognitive therapies for children and adolescents have generally favorable, but probably nonspecific effects on behavior. On the other hand, the specific effects, however, were weak overall. Therapeutic benefit has been demonstrated only for certain individual types of therapy for specific indications.

## 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 (TMTA), and trail-making test B (TMTB). 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.

# 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.

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

Metaanalysis



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.

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



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.

# Attention and Working Memory Training: The Effect of RehaCom Software on Cognitive Skills in a Non-Clinical Sample



Barbu MC, Furlong RM, Poveda B, Scotland J

Psychol Behav Sci Int J; Volume 4 Issue 3 - June 2017, DOI:10.19080/PBSIJ.2017.04.555638

**Objective:** The present study investigated the efficacy of RehaCom, a computerized cognitive training program, in improving memory and attention functions in the healthy, adult brain in comparison to playing a simple game (Solitaire).

**Method:** 57 healthy participants completed either 9 sessions of attention and memory training within RehaCom or a simple game (Solitaire), for 30 minutes, 3 times a week for 3 weeks. Five pre- and post-training neuropsychological assessments were used to measure attention and memory, and level of anxiety and depression.

**Results:** Results showed no significant differences between the experimental group and the active

control group. Both groups showed a non-significant improvement in attention and memory over time as shown on scores in post-training assessments. This result indicated that, although both groups improved in terms of memory and attention function, RehaCom did not play a role in this improvement. However, participants in the experimental group showed a steady improvement over training sessions.

**Conclusion:** The study presents the novelty of testing RehaCom in a healthy population and the finding that it does not greatly improve memory and attention functions in a selection of healthy individuals. Further research is needed in order to assert its efficacy in improving cognitive functions across both healthy and patient populations.



## Stress-related cortisol responsivity modulates prospective memory

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Neuroendocrinology

Glienke K, Piefke M

Journal of Neuroendocrinology 2017 Dec;29(12). doi: 10.1111/jne.12544.

It is known that there is inter-individual variation in behavioural and physiological stress reactions to the same stressor. The present study aimed to examine the impact of cortisol responsivity on performance in a complex real life-like prospective memory (PM) paradigm by a re-analysis of data published previously, with a focus on the taxonomy of cognitive dimensions of PM. Twenty-one male subjects were stressed with the Socially Evaluated Cold Pressor Test (SECPT) before the planning of intentions. Another group of 20 males underwent a control procedure. Salivary cortisol was measured to assess the intensity of the biological stress response. Additionally, participants rated the subjective experience of stress on a 5-point rating scale. Stressed participants were post-hoc differentiated in high ( $n = 11$ ) and low cortisol responders ( $n = 10$ ). Cortisol niveau differed significantly between the two groups, whereas subjective stress ratings did not. PM performance

of low cortisol responders was stable across time and the PM performance of controls declined. High cortisol responders showed a nominally weaker PM retrieval across the early trials and significantly improved only on the last trial. The data demonstrate for the first time that participants with a low cortisol responsivity may benefit from stress exposure before the planning phase of PM. PM performance of high cortisol responders shows a more inconsistent pattern, which may be interpreted in the sense of a recency effect in PM retrieval. Alternatively, high cortisol responses may have a deteriorating effect on PM retrieval, which disappeared on the last trials of the task as a result of the decrease of cortisol levels across time. Importantly, the data also demonstrate that the intensity of cortisol responses does not necessarily correspond to the intensity of the mental experience of stress.

## Acute social stress before the planning phase improves memory performance in a complex real life-related prospective memory task

Neurobiology of  
Learning and Memory

Glienke K, Piefke M

Neurobiol Learn Mem. 2016 Sep;133:171-81. doi: 10.1016/j.nlm.2016.06.025. Epub 2016 Jun 28.

Successful execution of intentions, but also the failure to recall are common phenomena in everyday life. The planning, retention, and realization of intentions are often framed as the scientific concept of prospective memory. The current study aimed to examine the influence of acute stress on key dimensions of complex „real life“ prospective memory. To this end, we applied a prospective memory task that involved the planning, retention, and performance of intentions during a fictional holiday week. Forty healthy males participated in the study. Half of the

subjects were stressed with the Socially Evaluated Cold Pressor Test (SECPT) before the planning of intentions, and the other half of the participants underwent a control procedure at the same time. Salivary cortisol was used to measure the effectiveness of the SECPT stress induction. Stressed participants did not differ from controls in planning accuracy. However, when we compared stressed participants with controls during prospective memory retrieval, we found statistically significant differences in PM across the performance phase.

Participants treated with the SECPT procedure before the planning phase showed improved prospective memory retrieval over time, while performance of controls declined. Particularly, there was a significant difference between the stress and control group for the last two days of the holiday week. Interestingly, control participants showed significantly better performance for early than later learned items, which could be an

indicator of a primacy effect. This differential effect of stress on performance was also found in time- and event-dependent prospective memory. Our results demonstrate for the first time, that acute stress induced before the planning phase may improve prospective memory over the time course of the performance phase in time- and event-dependent prospective memory. Our data thus indicate that prospective memory can be enhanced by acute stress.

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

PNAS

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.



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