

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).

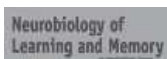
METHODS: 38 patients with MS and cognitive impairment on the Brief International Cognitive Assessment for MS (BICAMS) were enrolled. Patients were randomised to undergo 45 minutes of computerized cognitive rehabilitation using RehaCom software ($n = 19$) three times weekly for six weeks or to a control 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.

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



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.

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: Δ MMSE: $F = 6.251$, $P = .013$; Δ MoCA: $F = 4.991$, $P = .027$; and Δ 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 HW, 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.

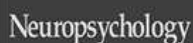
SUBJECTS AND METHODS: Forty-four participants were randomly allocated to the NFB (n=14), CACR (n=14), or control (CON) (n=16) groups. Two expert therapists provided the NFB, CACR, and CON groups with traditional rehabilitation therapy in 30-minute sessions, 5 times a week, for 6 weeks. NFB training was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

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



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.

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.

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

Journal of
Clinical and Experimental
Neuropsychology

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

Journal of Physical Therapy Science
This Journal For Authors Submissions

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



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.

CONCLUSION: Combined treatment of working memory training with exercises in semantic structuring is an effective method for cognitive rehabilitation of organic memory impairment.

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.

Effectiveness of Cognitive Rehabilitation Following Acquired Brain Injury: A Meta-Analytic Re-Examination of Cicerone et al.'s

Neuropsychology

Rohling ML, Faust ME, Beverly B, Demakis G

Neuropsychology. 2009 Jan; 23(1):20-39. doi: 10.1037/a0013659.

The present study provides a meta-analysis of cognitive rehabilitation literature ($K = 115$, $N = 2,014$) that was originally reviewed by K. D. Cicerone et al. (2000, 2005) for the purpose of providing evidence-based practice guidelines for persons with acquired brain injury. The analysis yielded a small treatment effect size ($ES = .30$, $d (+)$ statistic) directly attributable to cognitive rehabilitation. A larger treatment effect ($ES = .71$) was found for single-group pretest to posttest outcomes; however, modest improvement was observed for non-treatment control groups as well ($ES = .41$). Correction for this effect, which was not attributable to cognitive

treatments, resulted in the small, but significant, overall estimate. Treatment effects were moderated by cognitive domain treated, time post-injury, type of brain injury, and age. The meta-analysis revealed sufficient evidence for the effectiveness of attention training after traumatic brain injury and of language and visuospatial training for aphasia and neglect syndromes after stroke. Results provide important quantitative documentation of effective treatments, complementing recent systematic reviews. Findings also highlight gaps in the scientific evidence supporting cognitive rehabilitation, thereby indicating future research directions.

Evidence-based cognitive rehabilitation: updated review of the literature from 1998 through 2002

Archives of Physical Medicine and Rehabilitation

Cicerone KD, Dahlberg C, Malec JF, Langenbahn DM, Felicetti T, Kneipp S, Ellmo W, Kalmar K, Giacino JT, Harley JP, Laatsch L, Morse PA, Catanese J; Arch Phys Med Rehabil. 2005 Aug; 86(8):1681-92.

OBJECTIVE: To update the previous evidence-based recommendations of the Brain Injury Interdisciplinary Special Interest Group of the American Congress of Rehabilitation Medicine for cognitive rehabilitation of people with traumatic brain injury (TBI) and stroke, based on a systematic review of the literature from 1998 through 2002.

DATA SOURCES: PubMed and Infotrieve literature searches were conducted using the terms attention, awareness, cognition, communication, executive, language, memory, perception, problem solving, and reasoning combined with each of the terms rehabilitation, remediation, and training. Reference lists from identified articles were reviewed and a bibliography listing 312 articles was compiled.

STUDY SELECTION: One hundred eighteen articles were initially selected for inclusion. Thirty-one studies were excluded after detailed review. Excluded articles included 14 studies without data, 6 duplicate publications or follow-up studies, 5 non-treatment studies, 4 reviews, and 2 case studies involving diagnoses other than TBI or stroke.

DATA EXTRACTION: Articles were assigned to 1 of 7 categories reflecting the primary area of intervention: attention; visual perception; apraxia; language and communication; memory; executive functioning, problem solving and awareness; and comprehensive-holistic cognitive rehabilitation. Articles were abstracted and levels of evidence determined using specific criteria.

DATA SYNTHESIS: Of the 87 studies evaluated, 17 were rated as class I, 8 as class II, and 62 as class III. Evidence within each area of intervention was synthesized and recommendations for practice standards, practice guidelines, and practice options were made.

CONCLUSIONS: There is substantial evidence to support cognitive-linguistic therapies for people with language deficits after left hemisphere stroke. New evidence supports training for apraxia after left hemisphere stroke. The evidence supports visuospatial rehabilitation for deficits associated with visual neglect after right hemisphere stroke. There is substantial evidence to support cognitive

rehabilitation for people with TBI, including strategy training for mild memory impairment, strategy training for post-acute attention deficits, and interventions for functional communication deficits. The overall analysis of 47 treatment comparisons, based on class I studies included in the current and previous review, reveals a differential benefit in favor of cognitive rehabilitation in 37 of 47 (78.7%) comparisons, with no comparison demonstrating a benefit in favor of the alternative treatment condition. Future research should move beyond the simple question of whether cognitive rehabilitation is effective, and examine the therapy factors and patient characteristics that optimize the clinical outcomes of cognitive rehabilitation.

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.

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, WCSTte 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.

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 ($F = 4015p < .05$, $Eta = 0.242$), Wds ($F = 11.806$, $p < .05$, $Eta = .48$) PRMQ1 ($F = 3.314$, $p < .05$, $Eta = 0.20$) PRMQ7 ($F = 2.85$, $p < .05$, $Eta = 0.18$).

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, 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 endophenotypica 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 and specificity of computer-assisted cognitive remediation in schizophrenia: a meta-analytical study

**PSYCHOLOGICAL
MEDICINE**

Grynszpan O, Perbal S, Pelissolo A, Fossati P, Jouvent R, Dubal S, Perez-Diaz F
Psychol Med. 2011 Jan; 41(1):163-73. doi: 10.1017/S0033291710000607. Epub 2010 Apr 12.

BACKGROUND: Cognitive remediation is frequently based on computerized training methods that target different cognitive deficits. The aim of this article was to assess the efficacy of computer-assisted cognitive remediation (CACR) in schizophrenia and to determine whether CACR enables selective treatment of specific cognitive domains.

METHOD: A meta-analysis was performed on 16 randomized controlled trials evaluating CACR. The effect sizes of differences between CACR and control groups were computed and classified according to the cognitive domain assessed. The possible influences of four potential moderator variables were examined: participants' age,

treatment duration, weekly frequency, and control condition type. To test the domain-specific effect, the intended goal of each study was determined and the effect sizes were sorted accordingly. The effect sizes of the cognitive domains explicitly targeted by the interventions were then compared with those that were not.

RESULTS: CACR enhanced general cognition with a mean effect size of 0.38 [confidence interval (CI) 0.20-0.55]. A significant medium effect size of 0.64 (CI 0.29-0.99) was found for Social Cognition. Improvements were also significant in Verbal

Memory, Working Memory, Attention/Vigilance and Speed of Processing with small effect sizes. Cognitive domains that were specifically targeted by the interventions did not yield higher effects than those that were not.

CONCLUSIONS: The results lend support to the efficacy of CACR with particular emphasis on Social Cognition. The difficulty in targeting specific domains suggests a 'non-specific' effect of CACR. These results are discussed in the light of the possible bias in remediation tasks due to computer interface design paradigms.

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.

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



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



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.

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 neuro-modulatory 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.

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



Semkovska M, Ahern E, Lonergán 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.

