MASKUN NEUROLOGINEN KUNTOUTUSKESKUS

RIMS | REHABILITATION IN MULTIPLE SCLEROSIS

Neuropsychological aspects of MS – is rehabilitation needed?

Päivi Hämäläinen, PhD, Ajunct professor

Cognitive deficits are typical in MS

- Both permanent and temporary cognitive impairments are related to MS
- Permanent deficits in 50-60% of patients due to
  - Variable changes in the CNS
- Temporary deficits in most patients due to
  - Depression, mood problems
  - Relapses (cognitive relapses)
  - Fatigue

Approximately 60% of PwMS have permanent cognitive impairments:

Impairment	Frequency
Memory, new learning	**30 – 50 %**
Information processing	**30 – 50 %**
Attention, working memory	**25 – 35 %**
Executive functions	**20 – 30 %**
Visual perception, word fluency	10 – 20 %
Severe, widespread cognitive decline	app. 10 %

Combined from several sources

There is no single profile of cognitive deficits in MS.

Cognitive deficits cannot be predicted

- Relationship between disease duration, physical disability and disease course weak , modest or unclear

  →cognitive deficits may appear already at the early stages

  →physical and cognitive functioning do not go hand by hand

  →cognitive deficits are related to all disease types although patients with progressive disease course often manifest more problems than those with relapsing disease

High cognitive reserve probably protects from CI!?

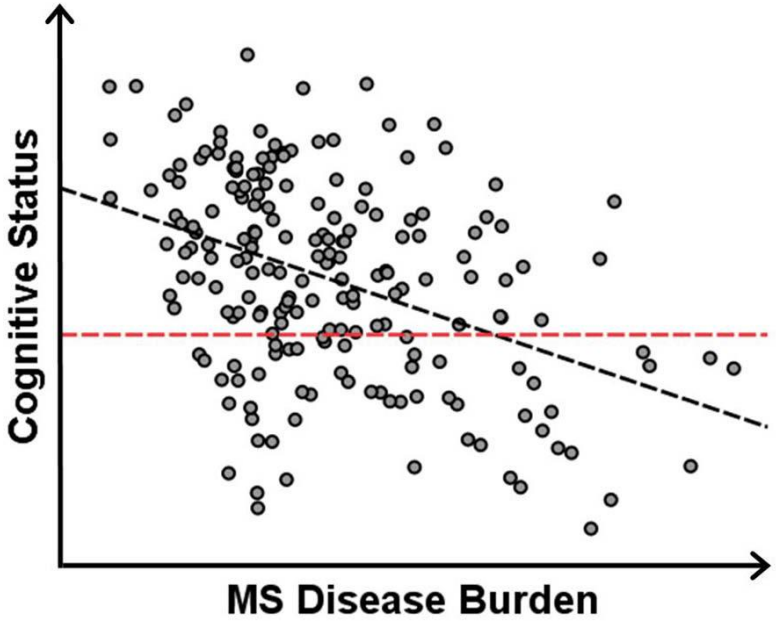


Figure 1. Schematic of the negative relationship between MS disease burden and cognitive status, with notable variability around the regression line. Data points within this schematic are not derived from any specific set of data, but are meant to represent the typical relationship observed between cognitive status (e.g., cognitive efficiency) and MS disease burden (e.g., brain atrophy). The red line marks 1.5 standard deviations below normative expectations, which is a typical benchmark for cognitive impairment.

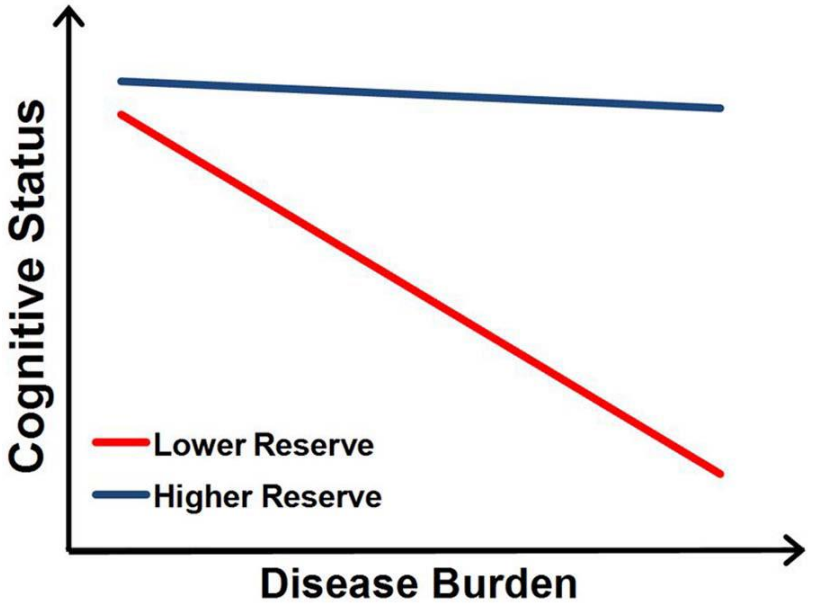


Figure 2. Schematic of the interaction between reserve (maximal lifetime brain growth (MLBG), intellectual enrichment) and disease burden on cognitive status, whereby higher reserve attenuates the negative impact of disease on cognition.

Sumowski & Leavitt, 2013

Cognitive impairments may progress

- In mediate lenght follow-ups (1-4 years), individual variability typical, defined cognitive decline is a risk factor for further deterioration

- In longer (4-10 years) follow-ups, cognitive decline typically progresses and comes more widespread

Every effort should be taken to slow down the progression

Rehabilitation is necessary

…because cognitive impairments have been shown to affect:

- personal competence, self-esteem, quality of life
- employment
- driving skills
- social activities
- emotional wellbeing and physical independence
- rehabilitation outcome
- caregiver wellbeing

… and medications do not treat cognitive impairments

… and results on rehabilitation are mainly positive

- Two Cochrane reviews show preliminary eveidence (2014 and 2016)
- According to a data search conducted in October 2016 (appeco.net)
  - 40 randomised controlled studies on neuropsychological / cognitive rehabilitation in MS
    - Half of studies on cognitive training alone
    - Half on more multimodal / holistic neuropsychological rehabilitation (information, feedback, learning strategies and compensations etc.)
- In 39/40 studies at least part of the outcomes positive

Cochrane Library
Cochrane Database of Systematic Reviews

Neuropsychological rehabilitation for multiple sclerosis (Review)

Rosti-Otajärvi EM, Hämäläinen PI

Rosti-Otajärvi EM, Hämäläinen PI.
Neuropsychological rehabilitation for multiple sclero
Cochrane Database of Systematic Reviews 2014, Issue
DOI: 10.1002/14651858.CD009131.pub3.

www.cochranelibrary.com

2014: 20 RCT studies, 986 participants

Authors' conclusions

This review found low-level evidence for positive effects of neuropsychological rehabilitation in MS. The interventions and outcome measures included in the review were heterogeneous, which limited the comparability of the studies. New trials may therefore change the strength and direction of the evidence.

Cochrane Library
Cochrane Database of Systematic Reviews

Memory rehabilitation for people with multiple sclerosis (Review)

das Nair R, Martin KJ, Lincoln NB

das Nair R, Martin KJ, Lincoln NB.
Memory rehabilitation for people with multiple
Cochrane Database of Systematic Reviews 2016
DOI: 10.1002/14651858.CD008754.pub3.

www.cochranelibrary.com

2016: 15 RCT studies, 989 participants

Authors' conclusions

There is some evidence to support the effectiveness of memory rehabilitation on memory function, as well as on quality of life. However, the evidence is limited and does not extend to subjective reports of memory functioning or mood. Furthermore, the objective measures used are not ecologically valid measures, and thus potentially limit generalisability of these findings into daily life. Further robust RCTs of high methodological quality and better quality of reporting, using ecologically valid outcome assessments, are still needed.

Review Article

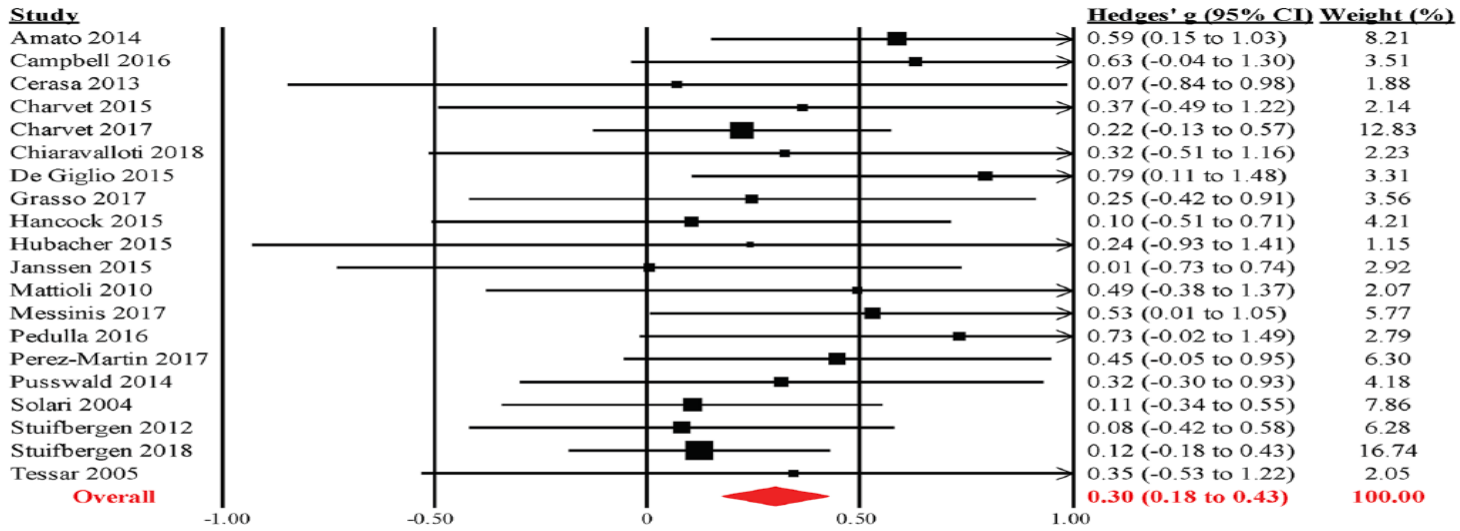
ASNR AMERICAN SOCIETY OF NEUROREHABILITATION

Neurorehabilitation and Neural Repair
2019, Vol. 33(9) 695–706

DOI: 10.1177/1545968319860490
journals.sagepub.com/home/nnr
SAGE

Computerized Cognitive Training in Multiple Sclerosis: A Systematic Review and Meta-analysis

Amit Lampit, PhD[1,2,3,4], Josephine Heine, MSc[2], Carsten Finke, MD[2,3], Michael H. Barnett, MBBS, PhD[4], Michael Valenzuela, MBBS, PhD[4], Anna Wolf, PhD[1], Isabella H. K. Leung, MBMSc[4,*], and Nicole T. M. Hill, MBMSc[1,*]



further training. *Conclusions*. CCT is efficacious for overall and key cognitive domains in adults with MS, but efficacy on other outcomes and in progressive subtypes remains unclear. Long-term and well-powered trials with diverse cohorts are needed to optimize and maintain the efficacy of CCT, investigate transfer to daily living, and determine who can benefit and whether CCT is a cost-effective strategy to attenuate cognitive decline in MS.

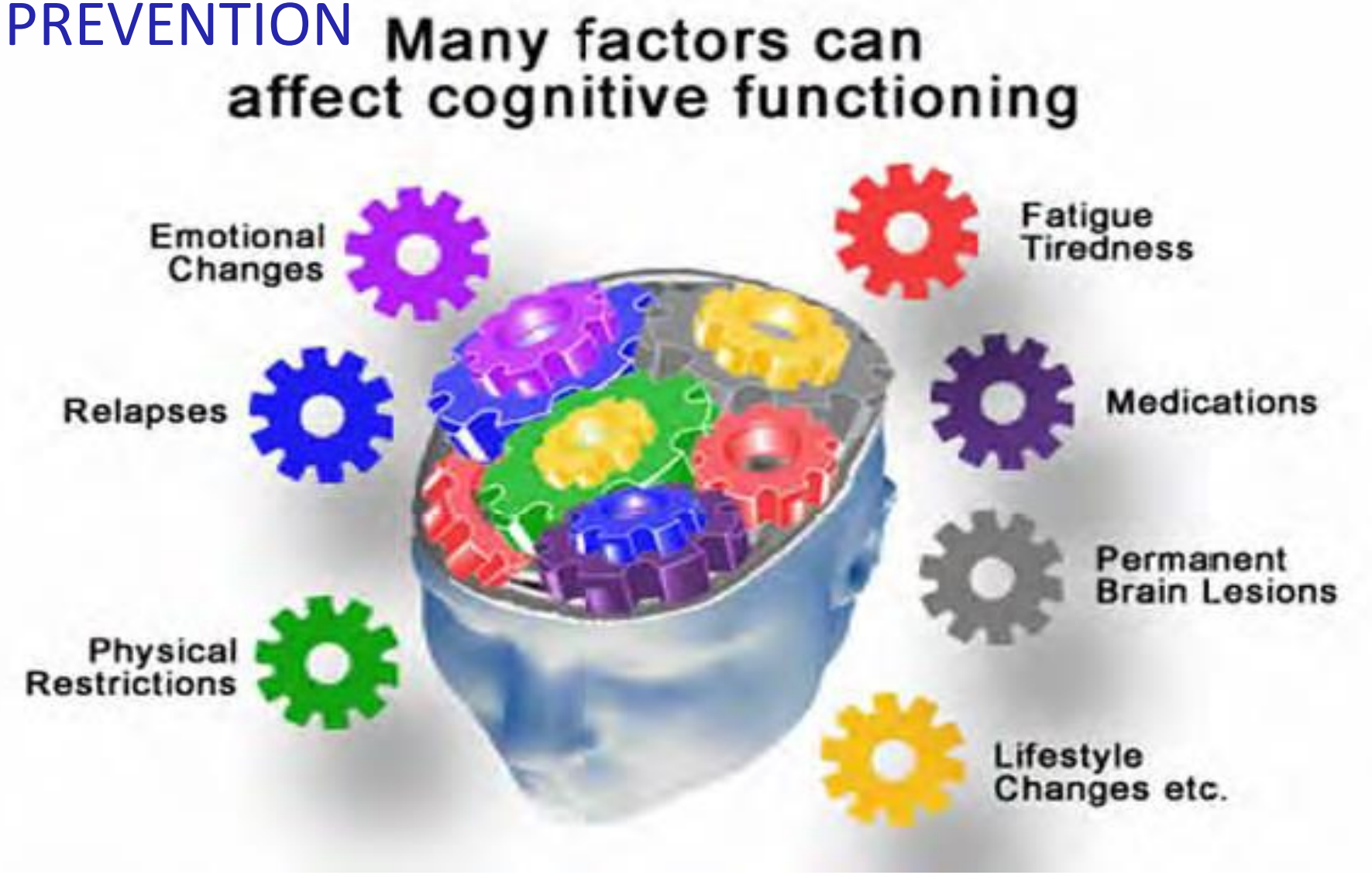
MASKUN NEUROLOGINEN
KUNTOUTUSKESKUS

RIMS | REHABILITATION IN MULTIPLE SCLEROSIS

How should rehabilitation be conducted?

Method	Aim	Target
Information / Prevention	To enhance the use of cognitive abilities, support cognitive reserve	Each patient
Restoration	To improve cognitive performance through cognitive training	Patients with mild/ focused deficits
Compensation	To compensate existing cognitive impairments by using internal / external startegies	Patients with more widespread deficits
Support / counselling	To understand one's cognitive strengths and weaknesses and take them into account in daily life	Patients with cognitive deficits Pts's nearest ones

PREVENTION



Information on the factors affecting cognition and on the significance of physical and cognitive activity in supporting brain reserve and preventing cognitive decline is important!

RESTORATION - cognitive training

- Has been shown to improve the trained cognitive function (i.e memory, attention)
- Cognitive training has been shown to improve cerebral activation, connectivity, and neural plasticity
- Especially when cognitive problems are focused and patient motivated to train systematically
- Evidence especially from elderly people and other diseases that cognitive training combined with physical exercise may be effective especially for dualtask performance

ARTICLES

2013

An RCT to treat learning impairment in multiple sclerosis

The MEMREHAB trial

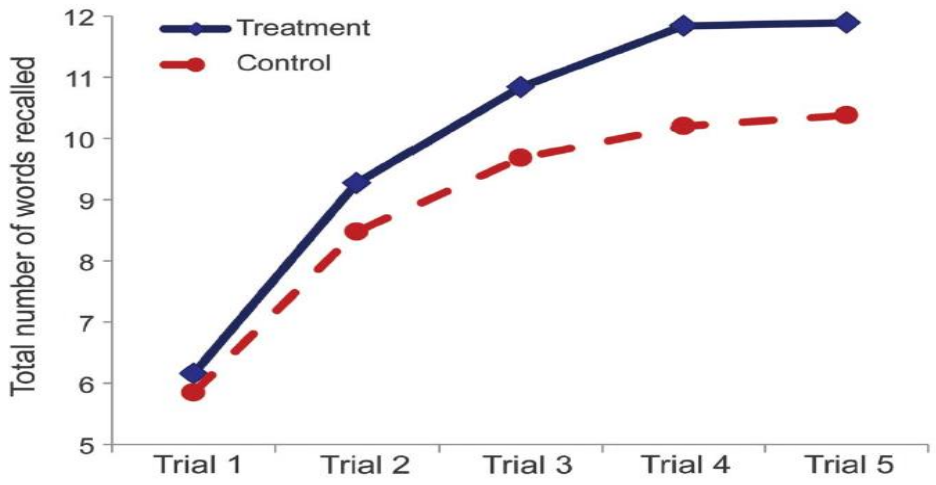
Nancy D. Chiaravalloti, PhD
Nancy B. Moore, MA
Olga M. Nikelshpur, PhD
John DeLuca, PhD

ABSTRACT

Objective: To examine the efficacy of the modified Story Memory Technique (mSMT), a 10-session behavioral intervention teaching context and imagery to facilitate learning, to improve learning and memory abilities in persons with multiple sclerosis (MS).

Methods: This double-blind, placebo-controlled, randomized clinical trial included 86 participants

Figure 2 California Verbal Learning Test (CVLT) learning slope across the 5 learning trials of the CVLT immediately posttreatment, by treatment group ($p < 0.05$)



86 PwMS,
41 intervention arm
45 control arm

→ Learning training (5 weeks, twice / week, , 45-60 min; total 10 sessions) improves learning slope and every day memory, positive effects last at least 6 months

Modified Story Memory Technique

J Neurol (2012) 259:1337–1346
DOI 10.1007/s00415-011-6353-x

ORIGINAL COMMUNICATION

Increased cerebral activation after behavioral treatment for memory deficits in MS

Nancy D. Chiaravalloti · Glenn Wylie · Victoria Leavitt · John DeLuca

- fMRI analysis during performance of a memory task in a subgroup of 16 patients (8 in the treatment and 8 in the placebo group)
- After treatment, greater activation was observed in the treatment group, involving frontal, parietal, precuneus, parahippocampal regions and cerebellum

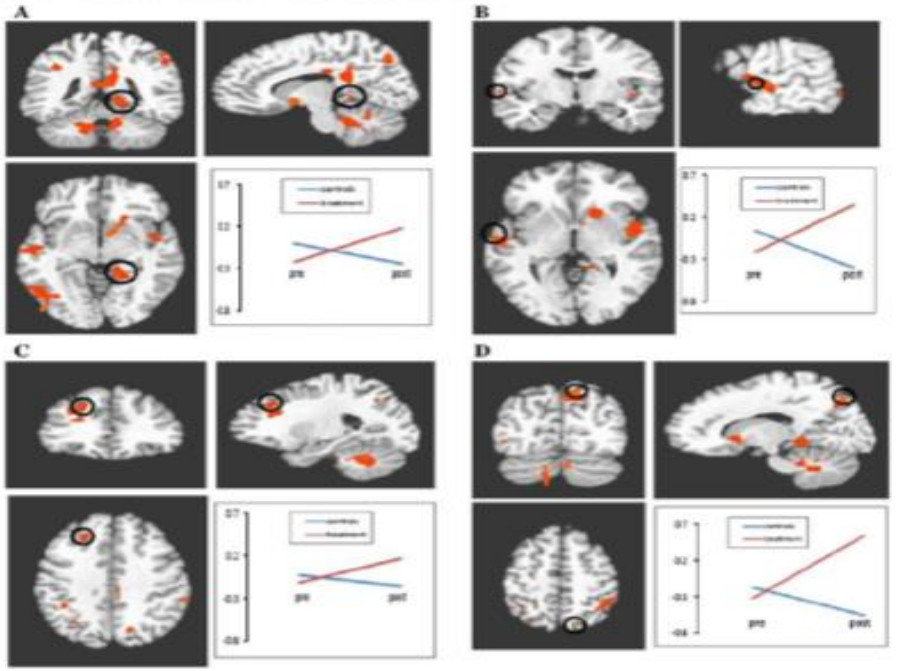
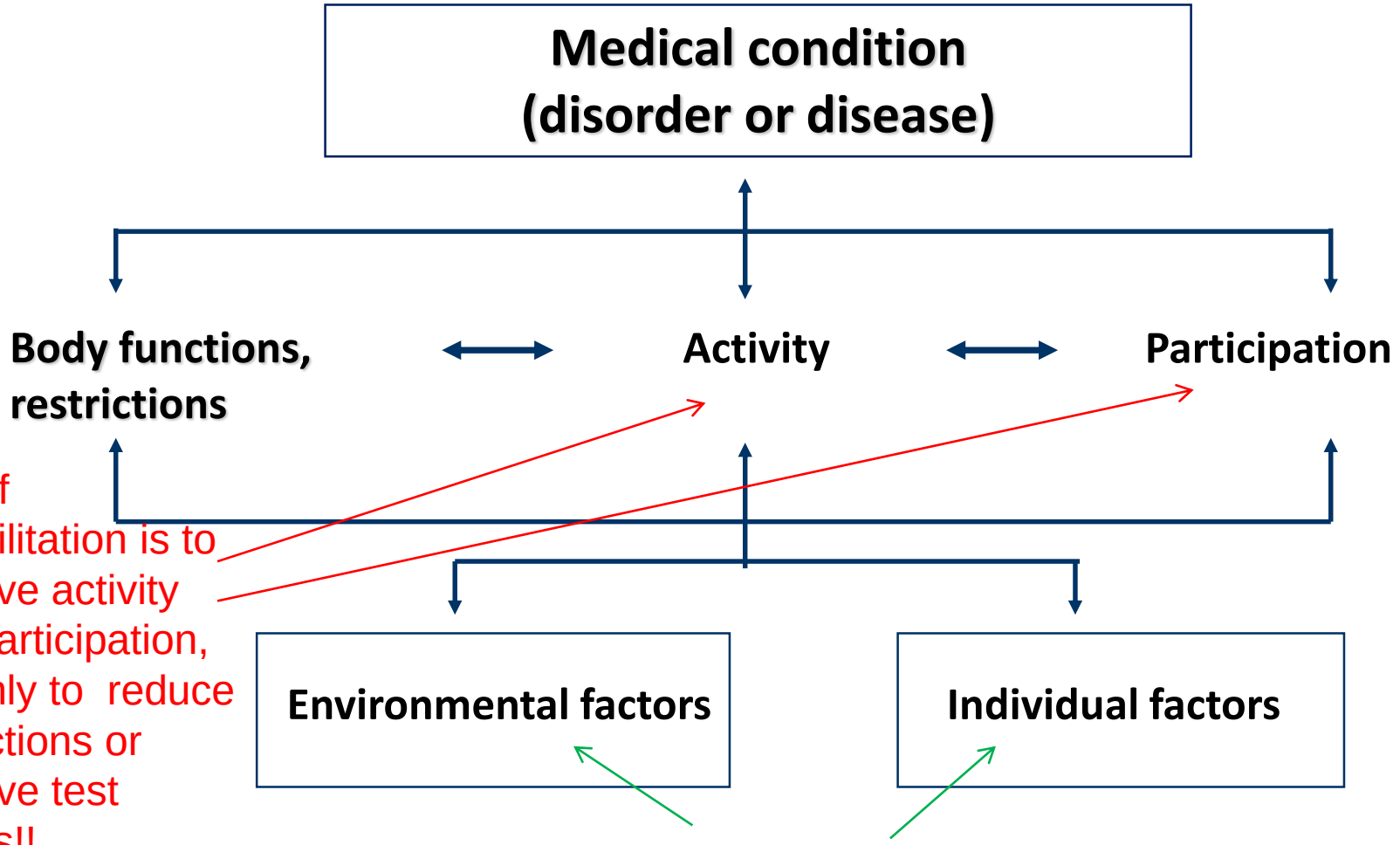


Fig. 2 Results of the 2 × 2 ANOVA with factors of time and group. Following treatment, significant increases in activation were seen in the treatment group relative to the control group in regions including frontal lobe, parietal lobe, and cerebellum. All comparisons are significant at $p < 0.01$ (minimum cluster size = 10 voxels). a Bold activation change from pre- to post-treatment in parahippocampal gyrus. Control group represented by *blue line*; treatment group represented by *red line*. All interactions shown are significant at $p < 0.01$. b Bold activation change from pre- to post-treatment in superior temporal gyrus. c Bold activation change from pre- to post-treatment in middle frontal gyrus. d Bold activation change from pre- to post-treatment in precuneus

COMPENSATION / Holistic approach is needed…

- Cognitive deficits are highly individual, often progressive and heterogeneous including emotional problems and cognitive fatigue
- It is important to learn strategies how to cope with affected cognitive functions
- Especially when cognitive impairments are more widespread, the aim is not to improve test performance but to support activity
- Therapist is needed to offer information, support understanding, promote adherence, and give feedback

ICF - classification



Aim of rehabilitation is to improve activity and participation, not only to reduce restrictions or improve test scores!!

At best, rehabilitation is based on patient's individual needs and relies on patient's strenghts and motivators!!

Kela Etelä-Pohjanmaan sairaanhoitopiiri MASKUN NEUROLOGINEN KUNTOUTUSKESKUS Tays

Finnish multicentre study

The effects of strategy-based neuropsychological rehabilitation in MS

Research Paper

MULTIPLE SCLEROSIS JOURNAL | MSJ

Multiple Sclerosis Journal
2014, Vol 20(1) 99–107

DOI: 10.1177/1352458513494487
msj.sagepub.com
SAGE

Neuropsychological rehabilitation does not improve cognitive performance but reduces perceived cognitive deficits in patients with multiple sclerosis: a randomised, controlled, multi-centre trial

Anu Mäntynen[1], Eija Rosti-Otajärvi[2], Keijo Koivisto[3], Arja Lilja[4], Heini Huhtala[5] and Päivi Hämäläinen[4]

Journal of the Neurological Sciences 334 (2013) 154–160

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Neuropsychological rehabilitation has beneficial effects on perceived cognitive deficits in multiple sclerosis during nine-month follow-up

Eija Rosti-Otajärvi [a,*], Anu Mäntynen [b], Keijo Koivisto [c], Heini Huhtala [d], Päivi Hämäläinen [e]

Disability and Rehabilitation
An international, multidisciplinary journal

http://informahealthcare.com/dre
ISSN 0963-8288 print/ISSN 1464-5165 online
Disabil Rehabil, Early Online: 1–8
 DOI: 10.3109/09638288.2014.991452

informa healthcare

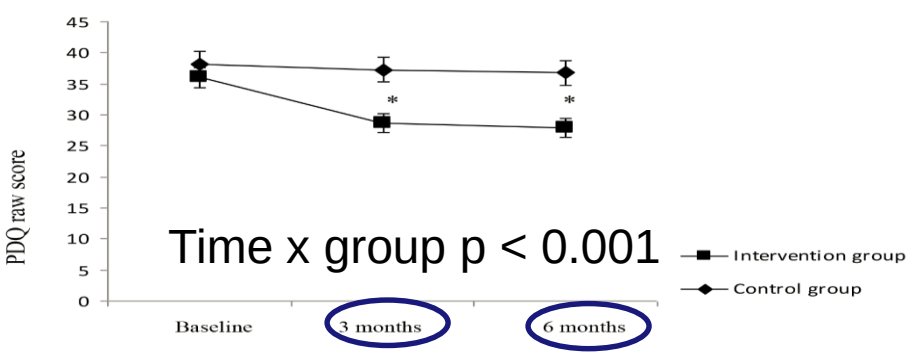
RESEARCH PAPER

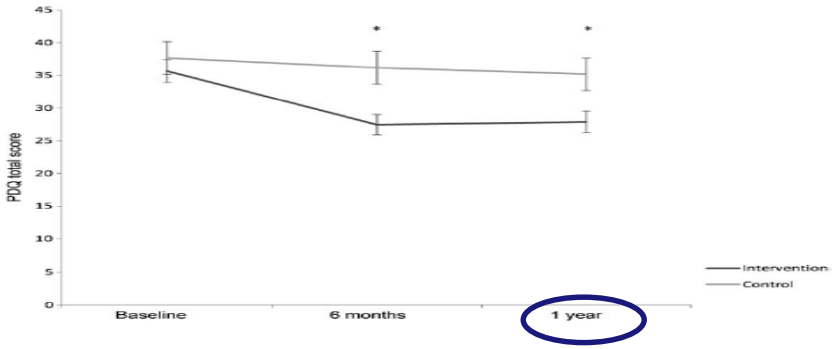
The use of goal attainment scaling in neuropsychological rehabilitation in multiple sclerosis

Mervi Rannisto[1], Eija Rosti-Otajärvi[1], Anu Mäntynen[2], Keijo Koivisto[3], Heini Huhtala[4], and Päivi Hämäläinen[5]

Teaching internal and external strategies to come along with attentional problems in daily life improved patients' self-perceived cognitive functioning although it did not improve cognitive test performance

Primary outcome: Perceived Deficits Questionnaire, sum score





Outcome 2: Symbol Digit Modalities Test (SDMT; total correct)

Baseline	3 months	6 months	Time x group
Intervention			
46.2±9.8	49.8±10.2	50.6±12.1	
Controls			p=0.316
45.5±8.4	47.5±8.4	48.2±8.2	

Outcome 3: Goal achievement (GAS, T-score)

Mean	SD	Median	Range	
Intervention				T = 50; goals achieved
56.2	8.5	56.0	41.0 – 75.0	at expected level

MASKU NEUROLOGICAL
REHABILITATION CENTRE

RIMS | REHABILITATION IN MULTIPLE SCLEROSIS

We have still a lot to do!

The quality of existing evidence is low

ACRM
AMERICAN CONGRESS OF REHABILITATION MEDICINE

Archives of Physical Medicine and Rehabilitation

journal homepage: www.archives-pmr.org

Archives of Physical Medicine and Rehabilitation 2017;98:353-67

REVIEW ARTICLE (META-ANALYSIS)

Rehabilitation in Multiple Sclerosis: A Systematic Review of Systematic Reviews

Fary Khan, MBBS, MD, FAFRM (RACP),[a,b,c] Bhasker Amatya, MD, MPH[a]

From the [a]Department of Rehabilitation Medicine, Royal Melbourne Hospital, Parkville, Victoria; [b]Department of Medicine, D Health Sciences, The University of Melbourne, Parkville, Victoria; and [c]School of Public Health and Preventive Medicine, Mon Melbourne, Victoria, Australia.

Intervention	No studies, participants	Inpatient	Community	Long-term survivorship	GRADE*
Multidisciplinary rehabilitation	9 RCTs, 1 CCT, 954				Moderate
Physical therapy	76 trials (45 RCTs)				High
Progressive resistance training	6 RCTs, 6 non-RCTs, 289				Low
Strength training	5 RCTs, 2 CCTs 249				Moderate
Exercise therapy (walking)	35 RCTs, 1255				High
Exercise therapy (fatigue)	60 RCTs, 2952				High
Physical therapy (balance)	11 RCTs, 340				Low
Exercise therapy (depression)	15 RCTs, 591				Low
Exercise therapy (cognition)	8 RCTs, 644				Low
Respiratory muscle training	15 trials (6 RCTs)				Low
Energy conservation	4 RCTs, 2 CCTs, 494				Moderate
HBOT	9 RCTs, 504				Low
WBV	11 RCTs, 314				Low
Electrical stimulation	1 RCT, 40				Very low
Hippotherapy	3 non-RCTs, 36				Very low
OT	96 trials				Low
Neuropsychological	20 RCTs, 986				Low
Cognitive rehabilitation	32 RCTs, 1527				Low
Cognitive Behavioural Therapy	7 RCTs				Moderate
Memory rehabilitation	8 RCTs, 521				Low
Dietary intervention (PUFAs)	6 RCTs, 794				Low
Dietary intervention (Vitamin D)	1 RCT, 49				Very low
Vocational rehabilitation	1 RCT, 1 CCT, 80				Low
Telerehabilitation	9 RCTs, 531				Low
Fatigue management programs	18 trials, 895				High
Upper limb rehab	41 trials (16 RCTs)				Low
Spasticity management interventions	9 RCTs, 341				Low

It is possible to rise the quality of the studies and improve evidence:

No	Recommendation
1	The use of comprehensive quality assessment criteria (e.g. Van Tulder 2003) as a guiding principle in preparing the research designs
2	Detailed reporting of the methods applied in the study (e.g. flow-charts including exact number of patients)
3	Sufficient sample sizes
4	Objective baseline assessment of the cognitive status of the patients
5	Evaluating treatment effects in cognitively homogeneous groups
6	Detailed reporting of the most essential disease variables
7	Determining the aim of the intervention beforehand and measuring it with the primary measure
8	Detailed reporting of the contents of the interventions
9	Detailed reporting of the basic statistics and outcome assessment timing
10	The use of such outcome measures which more extensively reflect everyday functioning and the generalization effects of the interventions, thus enabling the assessment of the achievement of individual rehabilitation aims related to everyday functions
11	Longitudinal follow-ups to evaluate the permanence of the treatment effects

Rosti-Otajärvi & Hämäläinen.Cochrane database 2014.

MASKU NEUROLOGICAL
REHABILITATION CENTRE

RIMS | REHABILITATION IN MULTIPLE SCLEROSIS

Take home message…

Synthesis based on existing studies:

TABLE 2 Ideas for the use of cognitive retraining and more multimodal rehabilitation approaches based on research findings and clinical experience

Cognitive retraining	Multimodal/holistic approach
For focused cognitive impairments	Probably enhances the effects of pure cognitive retraining
May improve cognitive test performance (especially memory and attention)	Does not improve test performance but may improve the ability to come along with cognitive deficits
Preferably intensive, several times/week	Positive results both from individual and group rehabilitation
Preferably specific to affected cognitive function	Should consist of feedback on strengths and weaknesses, strategy-based training, and learning of compensatory strategies
Feedback on training probably improves adherence and promotes better results	Probably best results when combined with a period of intensive cognitive training
May enhance functional brain reorganisation	May have positive effects on mood and feelings of fatigue

Rehabilitation should be personalised and based on the patient's needs

Progress of cognitive decline

Mild impairments → Severe impairments

Rehabilitation focus:

Patient's own resources, changes in one's own habits

information, NPS assessment, short-term NPS interventions – focus on strategy-oriented trainining

Environmental changes, aids

Longer-term holistic NPS interventions – focus on support, awareness, coping

Changes in other's attitudes

Account to the environment and activities of the patient

Support to the nearest ones and caregivers

Need for multiprofessional collaboration

You can now keep track on all the studies published in the field?

RIMS | REHABILITATION IN MULTIPLE SCLEROSIS

You can find information to support the decision on which approach is most suitable for a single patient

→ Take a look at appeco.net

Greetings from Masku Neurological Rehabilitation Centre

Thank you!

paivi.hamalainen@neuroliitto.fi