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:

<table>
<thead>
<tr>
<th>Impairment</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory, new learning</td>
<td>30 – 50 %</td>
</tr>
<tr>
<td>Information processing</td>
<td>30 – 50 %</td>
</tr>
<tr>
<td>Attention, working memory</td>
<td>25 – 35 %</td>
</tr>
<tr>
<td>Executive functions</td>
<td>20 – 30 %</td>
</tr>
<tr>
<td>Visual perception, word fluency</td>
<td>10 – 20 %</td>
</tr>
<tr>
<td>Severe, widespread cognitive decline</td>
<td>app. 10 %</td>
</tr>
</tbody>
</table>

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 in 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 length 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 evidence (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
**Neuropsychological rehabilitation for multiple sclerosis (Review)**

Rosti-Otajarvi EM, Hamalainen PL

*Rosti-Otajarvi EM, Hamalainen PL.
Neuropsychological rehabilitation for multiple sclerosis.
DOI: 10.1002/14651858.CD009131.pub3.

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.

**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 sclerosis.
Cochrane Database of Systematic Reviews 2016.
DOI: 10.1002/14651858.CD008754.pub3.

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

Amit Lampit, PhD1,2,3,4*, Josephine Heine, MSc2, Carsten Finke, MD2,3, Michael H. Barnett, MBBS, PhD3, Michael Valenzuela, MBBS, PhD4, Anna Wolf, PhD1, Isabella H. K. Leung, MBMSc4,* and Nicole T. M. Hill, MBMSc1,*

Tests for heterogeneity: $\chi^2$=1.42, df=19, $P=0.91$, $I^2=0.001$, $H^2=0$.
Test for overall random effect: $Z=4.721$, $P<0.001$.

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.
How should rehabilitation be conducted?
<table>
<thead>
<tr>
<th>Method</th>
<th>Aim</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information / Prevention</td>
<td>To enhance the use of cognitive abilities, support cognitive reserve</td>
<td>Each patient</td>
</tr>
<tr>
<td>Restoration</td>
<td>To improve cognitive performance through cognitive training</td>
<td>Patients with mild/ focused deficits</td>
</tr>
<tr>
<td>Compensation</td>
<td>To compensate existing cognitive impairments by using internal / external strategies</td>
<td>Patients with more widespread deficits</td>
</tr>
<tr>
<td>Support / counselling</td>
<td>To understand one’s cognitive strengths and weaknesses and take them into account in daily life</td>
<td>Patients with cognitive deficits Pts’s nearest ones</td>
</tr>
</tbody>
</table>
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
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.
Increased cerebral activation after behavioral treatment for memory deficits in MS

Nancy D. Chiaravalloti • Glen 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
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

Medical condition (disorder or disease)

Body functions, restrictions

Activity

Participation

Environmental factors

Individual factors

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

Anu Mäntynen¹, Elja Rosti-Otajärvi², Keijo Koivisto³, Arja Lilja⁴, Heini Huhtala⁵ and Päivi Hämäläinen⁶

Journal of the Neurological Sciences 314 (2013) 154–160
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)

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>46.2±9.8</td>
<td>45.5±8.4</td>
</tr>
<tr>
<td>3 months</td>
<td>49.8±10.2</td>
<td>47.5±8.4</td>
</tr>
<tr>
<td>6 months</td>
<td>50.6±12.1</td>
<td>48.2±8.2</td>
</tr>
<tr>
<td>Time x group</td>
<td>p=0.316</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>Range</th>
<th>T = 50; goals achieved at expected level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>56.2</td>
<td>8.5</td>
<td>56.0</td>
<td>41.0 – 75.0</td>
<td></td>
</tr>
</tbody>
</table>
We have still a lot to do!
The quality of existing evidence is low.
It is possible to rise the quality of the studies and improve evidence:

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

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

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

**Progress of cognitive decline**

- **Mild impairments**
  - Patient’s own resources, changes in one’s own habits
  - Environmental changes, aids

- **Severe impairments**
  - Changes in other’s attitudes

**Rehabilitation focus:**

- Patient’s own resources, changes in one’s own habits
  - Information, NPS assessment, short-term NPS interventions – focus on strategy-oriented training

- 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?

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@neurolit.to.fi