



# **A Cognitive Manual**

**Good neuropsychological  
practice in MS**

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Psychology and Neuropsychology**

## **COGNITIVE MANUAL**

### **GOOD NEUROPSYCHOLOGICAL PRACTICE IN MS**

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## **1. COGNITION IN MS – GOOD TO KNOW**

Cognitive problems are related to MS (both permanent and temporary deficits are frequent). 45 - 65% of people with multiple sclerosis (MS) have cognitive deficits in varying degrees of severity. MS related cognitive deficits are highly individual and may be progressive as is the disease itself. Because MS lesions interfere with the efficient functioning of the neural network, the most vulnerable cognitive domains are: attention, learning and memory, planning, problem solving, flexibility, mental speed and word finding. Taking into considerations the high frequency of cognitive deficits in MS and their serious consequences, information about MS related cognitive problems, neuropsychological assessment and feedback and not least neurocognitive rehabilitation should be offered as an part of any rehabilitation package. Neuropsychologists should be a part of any MS-team in order to be able to offer competent assessment and treatment to anyone diagnosed with MS.

The appearance of cognitive impairment cannot be predicted on the basis of other symptoms of the disease. Cognitive problems do not seem to be clearly related to such disease variables as duration of the disease or severity or type of the disease. Cognitive deficits may occur during the early stages of the disease as well as later on, in mildly or severely disabled patients. Cognitive impairments have no known links to any single physical symptom of MS. Sometimes dysarthria (poorly articulated speech), ataxia (problems with coordination) or nystagmus (rapid involuntary eye movements) maybe falsely interpreted as a sign of cognitive impairment. It has been found that cognitive deficits are more common in patients who have extensive cerebral demyelination or related neuropathological changes. Only quite little information exists about the progression of cognitive impairment in MS. It has been found that cognitive performances can vary during even short follow-up periods. Recent studies show that if people experience some cognitive problems, it is possible that they may become worse, although the rate of progression is individual and usually slow.

MS first causes is an irrecoverable loss of myelin, and then ultimately to the demise of the neurons thus exposed. Axonal damage and neuronal loss is thought to be an early feature of MS pathology (Anderson et al, 2009; Kim et al, 2010). Empirical evidence suggests that its accumulation may be the pathological correlate for the progression of disability. More recent evidence suggests a major role for neuronal loss in the cortical grey matter in MS (Magliozzi et al, 2007; Papadopoulos et al, 2009). Cognitive deficits are more often associated with secondary progressive MS and with a large cerebral lesion load. Whereas brain lesions can result in more permanent cognitive problems, a number of factors can temporarily interfere with or impair cognition. These factors include fatigue and tiredness, emotional changes, relapses, physical restrictions, drugs and lifestyle changes.

Like other symptoms of MS, cognitive problems vary greatly from person to person. Although MS is characterised by both white matter demyelination and perhaps to a lesser degree by grey matter changes of the central nervous system, a severe decline of general cognitive functioning (dementia) is rare in MS. The most typical cognitive impairments in MS include difficulties in memory and learning, attention, concentration and mental speed, problem solving (planning, performing and evaluating) and word finding. Most often problems are seen in one or two of these areas, whereas others function normally. There are many factors that can affect cognition in these include: fatigue, stress and anxiety, low mood, lack of sleep, excessive alcohol use, ageing and medications.

The PwMS might be experiencing cognitive changes but it might not be MS related and the above factors are actually the reason for the reported changes in cognitive ability. Also it is important to note these factors can also exacerbate underlying cognitive deficit. Therefore it is important these areas are considered in the assessment process.

Consequences of cognitive deficits

Cognitive deficits have a major impact psychosocially (education, work, driving, leisure activities, family and social life) and personally (personal competence, self-esteem, quality of life). Rehabilitation outcome is negatively influenced by cognitive deficits.

Cognitive problems can be extremely distressing. The associated practical problems, such as the effect on work, on social conversations, on the ability to manage one's own affairs, can threaten or even destroy social or work roles, self-confidence, or hopes for the present and the future, but in addition the meaning people give to cognitive problems can increase their distress. Cognitive problems might 'mean' 'I am afraid I'm going mad – I mustn't tell anyone, they won't like me/include me/love me any more'. They may be associated with an elderly relative's dementia, so the pwms fears becoming like their elderly relative. They may 'mean' 'I'm not able to work – people who can't work are useless and should be thrown on the scrap heap...' Such meanings are individual and can change if explored with a counsellor or psychologist.

Anxieties about relationships, already perhaps under threat from other MS symptoms, can be increased by cognitive problems, or by the fears associated with them. Those who live on their own, or who cannot trust their partners to take good care of them, may have good reason to fear their own mental deterioration. There may be little in the way of services available to help those under the age of 65 who have the cognitive deficits associated with MS, particularly if they show few other symptoms.

Cognitive problems can also affect the ability to grieve, which means that it can be hard for some people with MS to remain in touch with their own current reality and to give up the past. This in turn has effects on those around, who may become irritated or distressed with constantly having to reiterate the same reassurance or piece of information: 'no, you can't walk, even if they hadn't taken your crutches away, you still wouldn't be able to walk...' Flattening of emotions can also have a direct impact on relationships; partners may feel they are no longer important, no longer cared for or that the PwMS is no longer involved in the relationship.

It can be difficult to distinguish between ordinary crisis reactions and permanent cognitive difficulties. From time of diagnosis and through development of the disease there will be times where the person feels their integrity is so threatened that they will respond with crisis responses. In relation to PwMS and neuropsychological assessment it is worth noting that cognition is affected when a person is in crisis. Just when the crisis occurs, the thinking is to be characterized by chaos, there will be a focus on the experience that triggered the crisis and attention to other things will be disturbed. Also memory will be affected. Thinking will be simple and undifferentiated and problem solving very specific. As time passes and the person is adapting to what has happened, the cognitive functioning will return to normal. However, if the PwMS is cognitively affected, it may be difficult for them to process the dramatic change cognitively and it can be difficult for the person to get on with their life.

In addition to the cognitive changes noted in a crisis there will be a number of other reactions, that it also would be worth paying attention to from a neuropsychological perspective: emotional changes such as much anger and frustration and sadness, not to be mistaken for the lability, which may be a result of the MS. Also existential themes such as "why me?" and search for meaning will occur.

Cognitive problems can exacerbate other problems. Severe cognitive problems can lead to a partner feeling isolated and abandoned; for some people this is a serious problem with destructive consequences; others, however, in more secure relationships, perhaps with help from understanding professionals, find they can live with deteriorating mental capacities. While some aspects of the person remain intact, a partner may still be able to draw strength from their relationship, even if other sources of support have to be found.

Effect on relationships with healthcare professionals:

Accessing services may become a problem if mild cognitive problems mean that appointments are missed or the person becomes erratic or contradictory in their decision-making. Professionals are not always

aware of cognitive problems and may misread them as 'being difficult' or 'not bothering' for example. Defining goals, in particular, may become impossible, with damaging consequences for goal-led; service delivery. Occupational therapists as well as psychologists and counsellors can, however, be of help if problems are recognised.

## Medications

Medications have a part to play in cognition. Research conducted on DMTs shows that they can help slowing the progression of cognitive problems in MS. Although it is very controversial there has been research looking at medications for the symptomatic relief of cognitive deficits. However research is equivocal. Some of the medications used for symptomatic relief of other MS symptoms can produce side effects which mimic cognitive dysfunction.

### "Cognitive Reserve"

The concept of cognitive reserve dates from the 90's. Some authors noticed that, in several neurological diseases, the relation between brain modification and the consequences on the cognitive functioning on everyday life vary considerably from one individual to another (e.g. : Katzman R., Aronson M., Fuld P., Kawas C., Brown T., Morgenstern H., Frishman W., Gidez L., Eder H. & Ooi W.L., 1989). Then, a patient with high cognitive reserve, compared to a patient with low reserve, could sustain a higher degree of neural lesions before the appearance of the first symptoms of cognitive deterioration. Many factors may have an impact on that reserve. For example, a lot of studies conclude that a high school level (e.g. : Garibotto V., Borroni B. Kalbe E., Hernolz K., Salmon E, Holtoff V. Sorbi S., Cappa S.F., Padovani A., Fazio F. & Perani D., 2008 ; McDowell I, Xi G., Lindsay J. & Tierney M., 2007) a stimulating lifestyle (e.g. : Fritsch T, Smyth K.A., McClendon M.J., Ogrocki P.K., Santillan C., Larsen J.D. & Strauss M.E., 2005) and a high intelligence (e.g. : Stern Y., 2006) are associated with a decrease of the risk of dementia.

There are two models of cognitive reserve. The passive models hypothesize that anatomical inter-individual differences underlie the different levels of cognitive reserve. Concretely, it means that the cerebral volume, the number of neurons and the number of synapses may influence the level of the reserve (Satz P., 1993). The second models, the active ones, hypothesize that the differences between individuals depend on their ability to activate optimal cognitive processes or optimal neuronal network (Stern Y., 2009). Therefore people with a high cognitive reserve may activate more efficient and more flexible networks. Consecutively, they can recruit alternative network in case of cerebral lesion or neurological diseases. We can use the term "cognitive reserve" for brain and non-brain damaged individuals. However, the term "compensation" is more adequate following specific brain damages (Stern Y., 2002). Note that these models are not mutually exclusive and the combination of the two approaches might describe all the observations associated with the cognitive reserve concept (Stern Y., 2002).

Since a few years, some authors studied this concept related to multiple sclerosis. Several studies conclude that higher cognitive reserve may protect MS people from cognitive dysfunction (e.g. : Sumowski J.F., Chiaravalloti N. & DeLuca J., 2009 ; Benedict R.H., Morrow S.A., Weinstock Guttman B., Cookfair D. & Schretlen D.J., 2010 ; Sumowski J.S., Wylie, G.R., DeLuca, J. & Chiaravalloti, N., 2010). Again, the premorbid factors associated with the reserve levels are education, intelligence, vocabulary, etc. Following the study of Sumowski J.S. & al. (2010), Arnett P.A. (2010), suggest that "it would be reasonable to encourage patients with MS to engage in activities that might enhance cognitive reserve. Encouraging patients to engage in regular exercise, actively pursue social relationships, and engage in mentally stimulating activities might maintain or improve CR and help to buffer patients against the long-term cognitive effects of the disease."

## **2. NEUROPSYCHOLOGICAL ASSESSMENT**

### **2.1 What is neuropsychological assessment?**

A neuropsychological assessment helps to evaluate to what extent any reported cognitive problems are organic (as a result of damage to the brain) or a psychological reaction to the disease or its evolution.

Cognitive problems can be evaluated with a neuropsychological assessment and is based on neuropsychological tests as well as on an interview. By using it, the severity and characteristics of cognitive impairments can be evaluated individually. Furthermore, the individual strengths can be found and strategies to alleviate the effects of cognitive impairments can be suggested. Not everyone will necessarily need an extended neuropsychological assessment.

It is important in assessment to consider the person's motor, visual and verbal disabilities. All of these can have a significant impact on the overall assessment result. It may be necessary to adapt assessment tools in order to gain required information.

#### Neuropsychological assessment in research

Neuropsychological assessment has been employed for study purposes in evaluating the frequency, the characteristics and natural history of cognitive impairment as well as its relationships to other disease variables. Studies on cognitive functioning in MS have been able to show the effects of cognitive impairments on employment, driving skills, personal independence etc. Many recent studies have evaluated the effectiveness of medications and different rehabilitation methods on MS-related cognitive deficits. These kinds of studies have made it possible to develop methods to alleviate the effects of cognitive problems.

### **2.2 Neuropsychological assessment in clinical practice**

#### Why to do neuropsychological assessment

Cognitive deficits should be diagnosed as early as possible to be able to help patients and their care givers to cope with the new situation and to reduce the additional stresses and problems caused by misunderstanding of cognitive changes.

#### When to do neuropsychological assessment

As early as possible in the disease course as a baseline on which any future change is able to be measured.

When it is necessary to perform neuropsychological assessment:

- when evaluating working ability
- when evaluating driving ability
- when the patient has problems in coping with cognitive impairments
- to inform the patient about his her cognitive strengths and weaknesses to be able to cope with everyday demands

Not everyone will necessarily need a further neuropsychological assessment. Many people can identify for themselves the individual areas that are causing problems and work out ways to deal with them.

Assessment should not be completed during a relapse or if there is any acute psychological problem e.g. depression or anxiety – this should be treated where possible first. It is also important possible medication effects are taken into account.

### How to do neuropsychological assessment

It should depend on the purpose of the assessment. Neuropsychological assessment can be used for screening or as a comprehensive evaluation. It can also be used to monitor changes over time.

### Interview and preparation

Neuropsychological assessment is based on neuropsychological tests as well as on an interview. By using it, the severity and characteristics of cognitive impairments can be evaluated individually. Furthermore, the individual strengths can be found and strategies to alleviate the effects of cognitive impairments can be suggested. Not everyone will necessarily need a neuropsychological assessment.

In preparation of the neuropsychological assessment there should be an interview with the patient and a close relative, friend or cohabite.

### Questions to be posed:

- What cognitive difficulties are they experiencing (if any)
- Where or when, e.g. at work/home, time of day, have they noticed these difficulties
- Have they tried ways to manage these difficulties
- When they first notice the problems?
- Have the problems got worse over time – looking for rapid progression or slow progression
- Medications
- Lifestyle including smoker, alcohol use and illegal substance use
- Medical and psychiatric history
- Demographic information i.e. education and vocational history
- Family make up
- Birth, development
- Family history of neurological conditions including dementias

Insight in the patients metacognitive skills (patients self evaluation of the degree of deficits in the cognitive domain and his daily life) is useful because not every deficit or disorder poses a problem for the patient.

During the interview patients should be informed about the rationale, contents and time of the examination and consent should be obtained before the assessment is conducted.

### Testing

In this section the most commonly reported tests in the literature are reported. It is most important that tests appropriate to the reported cognitive difficulty are used. Tests will need to be relevant to local country and validated for the local culture and population.

Attention and information processing speed: STROOP, Trailmaking A+B, Delis Kaplan Executive Function Battery (DKEFS) – subtest Trails, Design Fluency; Paced Auditory Serial Addition Test (PASAT), Symbol Digit Modalities Test (SDMT), Concentration Task D2, Ruff 2 & 7, Selective Attention Task

Memory and Learning: Verbal: Rey 15-words, Californian Verbal Learning Test, Busschke Selective Reminding Test.

Visual: Complex Figure Test (Rey figure) immediate and delayed recall, 10/36 Spatial Recall Test, Both: Weschler Memory Scale-R /III/IV (WMS), Camden Memory Tests, Doors and People

Working memory: Brown Pterson, TAP, Digit Span, Spatial Span, Lottery subtest from The Test of Everyday Attention

Visuo-spatial-constructive: drawing (tree, 5-star, bicycle, house), clock drawing, Behavioural Inattention

Test (BIT), Hooper Visual Organisation Test, Benton, Visual Organisation and Spatial Perception (VOSP), Rey Complex Figure- copy

Executive functions: Winconsin Card Sorting Test, Frontal Assessment Battery (FAB), Hayling and Brixton, BADS, verbal fluency (animals, occupations, ) Mazes, Raven, Tower Of London. DKEFS, STROOP

Mood: Hospital Anxiety and Depression Scale (HADS), Mental Health Inventory (MHI)

Behavioural: Frontal Systems of Behavioural Evaluation (FrIsBE), DEX questionnaire from the BADS

Intellectual evaluation: WAIS-III/IV, WASI

Pre-morbid intellectual functioning: WTAR, Schonell,

Screening batteries: MMSE, BRIEF, RBANS, MACFIMS, RAO

### Feedback

Feedback is a very important part of the assessment process. It enables the clinician, together with the patient and any family member, to compare the results of PwMS self evaluation and the objective results of neuropsychological assessment. It ought to consist of the test performance, individual strengths and weaknesses, spared functions, effects of fatigue, psychological state, etc.

It is important to think about how the observed strengths and weaknesses are reflected in the patients' daily life. Questions needed to be asked about what the patient thinks about the findings and the effects of the findings on the patient.

Most importantly the patient and their family will want to know how to cope with the difficulties highlighted by the assessment, how they can improve their quality of life by reorganising their everyday activities. They also need to know which compensating strategies would be helpful if there are some gadgets that would be useful (like a personal organizer). They would also benefit from any advice about stress and energy management.

### **3. COGNITIVE FUNCTIONS AND REHABILITATION OF DIFFERENT COGNITIVE DOMAINS**

#### **3.1 What is neuropsychological rehabilitation?**

The basis of neuropsychological rehabilitation is always a comprehensive neuropsychological assessment, which has identified both the cognitive strengths and the weaknesses of the patient. Neuropsychological rehabilitation for MS patients aims at reducing the harmful effects of neuropsychological deficits caused by cerebral disturbance. Neuropsychological rehabilitation can be roughly divided into four approaches, which can flexibly be carried out in rehabilitation according to the situation (Kanninen 1997):

1. retraining of disturbed functions,
2. reorganising functions
3. promoting the use of preserved functions
4. learning compensation strategies

Holistic approach which takes into account widely PwMS cognitive, emotional, and psychosocial aspects, has been regarded as the best rehabilitation approach (Wilson 1997, 2008).

In rehabilitation efforts are set in to support the understanding of the PwMS and their caregiver/social network, or their spouse about disease-related neuropsychological problems and their best possible management in the context of everyday functions.

The effectiveness of neuropsychological rehabilitation

Cognitive deficits have a wide effect on the PwMS quality of life. The alleviation of the harmful effects caused by these deficits should therefore be a major goal of MS research. The effects of neuropsychological intervention may be seen in variables measuring cognitive performance, mood, fatigue, and social behavior.

There are studies which have evaluated the effects of neuropsychological rehabilitation on the patients' cognitive functioning and mood. A systematic literature review and quality analysis showed moderate evidence that direct memory and attention training can improve these cognitive functions in MS. Limited evidence was found that cognitive training has a positive effect on fatigue and mood. However, the meaning of the specificity of cognitive training to the outcomes remained unclear. Moderate evidence was found that multimodal neuropsychological rehabilitation including cognitive training and neuropsychological counselling (cognitive strategies and compensation) reduces cognitive and depressive symptoms in MS with some limited evidence that this kind of intervention reduces also subjective fatigue. Moreover, limited evidence was found that neuropsychological counselling and psychoeducation, which aim at improvement of social skills and behaviour control reduces behavioural problems in MS. Similarly, limited evidence was found that counselling carried out by nursing staff and systematic use of cognitive accessories (memory notebooks) may have positive effects on MS patients' mood.

Merely mechanical repetition of the information without cognitive rehabilitation strategies (e.g. increasing the organization) has not been found to be especially effective (Chiaravalloti 2003).

Overall, it seems that strategy-based memory rehabilitation by aimed at promoting everyday memory and attention is most successful (Hämäläinen & Rösti-Otajärvi, 2012).

In summary, although there is a profound need for studying the efficacy of cognitive rehabilitation programs and its impact on brain organization, a number of conclusions can be drawn from the studies already set up. Firstly, in order to be efficient, treatment should be high in frequency and last at least four to twelve weeks. Secondly, there is evidence for a shift in activation from the left to right hemisphere

during higher-order cognitive functions. Thirdly, studies focusing on functional reorganization after cognitive intervention need to control for spontaneous recovery and compensatory brain activity which occurs even at the earliest stages in MS.

### **3.2 Efficacy of cognitive intervention and its impact on the brain in MS**

Given the high prevalence of cognitive disturbances in pwMS and the possibility of motor rehabilitation, it is surprising to find such a low number of studies examining cognitive rehabilitation in multiple sclerosis. Further, the studies, which already exist, show methodological weaknesses.

For instance, Lincoln et al. (2002) randomized 240 MS-patients in three groups: a control group, an assessment group and a treatment group. The patients in the treatment group participated in a cognitive training concentrating on those functions which were classified as impaired in prior testing. There were no effects on neuropsychological outcome measures in the treatment group. However, although the training was supervised, it was low in frequency. Further, Solari et al. (2004) conducted a study investigating computer aid training focusing on attention and memory which included a control group receiving unspecific training. As in the study by Lincoln et al. (2007), no effect of the treatment was found. But, again, the groups were trained in low intensity (i.e. 16 training sessions during eight weeks), which might partially explain the lack of efficacy of the program. In fact, in a review Penner et al. (2007) concluded that cognitive training should last at least four to 12 weeks in order to be efficient on a behavioral basis. A second short-coming of the study by Lincoln et al. (2002) was the reliance on self-reported measurements at the end of the treatment phase to study its efficacy. These limitations were accounted for by a study of Hildebrandt et al. (2007) which investigated the efficacy of a high frequency home based computer training focusing on memory functions. Using a controlled study design, it turned out that the intervention was significantly successful in improving memory functions. Some cognitive short-comings appear to remit without explicit cognitive intervention. This spontaneous remission of cognitive deficits in MS has been reported in a number of studies. For instance, Staffen et al. (2002) reported the result of an fMRI-study with the visual analogue to the PASAT (i.e. the PVSAT). They found no difference in performance between healthy controls and pwMS, but an altered pattern of brain activation in the fMRI-study in the latter group. Additionally, Audoin et al (2003) observed a shift in activation from the left prefrontal cortex (PFC) to the corresponding areas in the right hemisphere during performance of a numeric verbal working- memory task (i.e. the PASAT).

In a more recent study, Audoin et al. (2008) showed that this effect was also observable at one year follow-up in that the higher the activation in the right PFC, the higher the level of performance on the PASAT. These studies indicate that spontaneous recovery of higher-order cognitive function occurs even at the earliest stage of MS and is able to compensate to a high degree for behavioral deficits.

Functional reorganization occurs which has the potential to keep cognitive functions on a high level for a longer time. As a consequence, it seems possible to use these mechanisms to advance cognitive rehabilitation with cognitive intervention program and to study its effects on brain functioning. But, the study of brain reorganization as a consequence of evidence- based cognitive intervention programs is still in its infancy. For instance, in a pilot-study Penner et al. (2005; 2006) investigated whether computer-based attention training has the potential to enhance brain functioning in MS. They found additional functional activity in brain areas responsible for a range of attention function. However, since the sample size was rather small, behavioral changes observed in this study cannot be generalized.

The effects of neuropsychological intervention may be seen in variables measuring cognitive performance, mood, fatigue, and social behavior. The treatment effects were observed in cognitive variables more often than in other evaluated variables. There are moderate evidence that direct memory and attention training can improve these cognitive functions in MS. Limited evidence was found that cognitive training has a

positive effect on fatigue and mood. Instead, the meaning of the specificity of cognitive training to the outcomes remained unclear. This is logical also in the context of heterogeneous MS-related cognitive deficits; to train a single cognitive function separated from everyday functions is not necessarily productive in a disease in which several cognitive domains can be affected. When expanding the evidence of memory rehabilitation to the studies not fulfilling the inclusion criteria of this review, it can be noticed that several studies have found that the so-called self-generation effect improves MS patients' memory and learning (Basso 2007; Chiaravalloti 2002; Goverover 2008; O'Brien 2007). The results concerning self-generation refer to the fact that material generated by the person him/herself seems to be better recalled than material given from outside. Moreover, self-generation has been demonstrated to improve MS patients' performance in concrete everyday functions (Activities of Daily Living) (Goverover 2008). On the other hand, merely mechanical repetition of the information without cognitive rehabilitation strategies (e.g. increasing the organization) has not been found to be especially effective (Chiaravalloti 2003). Overall, it seems that strategy-based memory rehabilitation by aimed at promoting everyday memory and attention is most successful (Hämäläinen & Rösti-Otajärvi).

When evaluating the effects of rehabilitation intervention, the aim should be to use measures which reflect, in addition to the severity of a symptom, also its effects on everyday activities, and how the patient copes with the symptom or problem. This is especially relevant in a progressive disease as the main aim of rehabilitation interventions may not be to reduce the severity of the symptom but to alleviate the effects of the symptom on everyday life, and to support the patient in coping with it. It is questionable whether the change in the cognitive test performance also reflects the real change in everyday functions when the rehabilitation is based on individual aims relating to everyday functions (Wilson 2008). Even in studies in which the main aim of the intervention is to teach compensatory strategies, the real benefits of the intervention do not necessarily become evident in outcome measures not reflecting the use of such strategies (Cicerone 2000). Ideally, measures should reflect meaningful functional improvements such as the use of compensatory strategies to fulfil real-life demands, performance in everyday 36 activities, changes in level of productivity, or measures of subjective well-being (Cicerone 2000). Future studies should include measures to evaluate more extensive functional capacity and, in this way, possibly uncover the generalization effects on the PwMS everyday functions. In addition to general measures, methods enabling us to measure the achievement of individual aims relating to everyday functions are needed (Hämäläinen & Rosti-Otajärvi).

In summary, although there is a profound need for studying the efficacy of cognitive rehabilitation programs and its impact on brain organization, a number of conclusions can be drawn from the studies already set up. Firstly, in order to be efficient, treatment should be high in frequency and last at least four to twelve weeks. Secondly, there is evidence for a shift in activation from the left to right hemisphere during higher-order cognitive functions. Thirdly, studies focusing on functional reorganization after cognitive intervention need to control for spontaneous recovery and compensatory brain activity which occurs even at the earliest stages in MS.

### **3.3 Neuropsychological rehabilitation in MS in clinical practice**

Why should be offered?

Given the prevalence of cognitive deficits in MS and the impact they have on patients' quality of life, it is important to treat cognitive problems in clinical practice. Cognitive deficits may have effect on physical independence, employment, social and recreational activities (Rao 1991b), driving skills (Kotterba 2003; Lincoln 2008), rehabilitation outcome (Langdon 1999) as well as caregiver strain (Chipchase 2001). If the patients with cognitive impairments do not know why cognition is affected and how to cope with them, they may have misconceptions about the reasons of their problems and what is going on with them. Therefore, cognitive problems, even mild ones, should be taken seriously and the possibility for treatment should be considered.

Because the systematic literature showed preliminary positive effects of neuropsychological rehabilitation on cognitive functioning, mood and fatigue, it should be considered as a main way to alleviate the effects of cognitive problems in MS.

When should be offered?

If the patient is motivated and have capacity to rehabilitation and neuropsychological assessment have revealed cognitive or behavioural deficits, even mild ones, neuropsychological rehabilitation should be considered as an option to help the patient to cope with the observed deficits.

The resources to offer neuropsychological rehabilitation vary a lot. There might not be resources to offer longterm individual neuropsychological rehabilitation to every patient with cognitive impairment, but the patients can have advantage also of shorter term counselling, psychological support and helping the patient to organise and structure daily activities.

How/what should be offered?

Because MS-related cognitive deficits are heterogeneous and their effects on PwMS functional capacity are individual, no single rehabilitation procedure can be employed to every patient. Therefore, neuropsychological rehabilitation has to be planned and carried out by taking into account the PwMS individual situation and needs. Accordingly, the rehabilitation can be emphasized to cognitive training, psychoeducation, or therapeutic support of the mental situation aiming at reducing the harmful, psychological effects of cognitive and/or behavioural problems.

The focus and contents of neuropsychological rehabilitation depends on the severity of the PwMS cognitive impairments. When cognitive problems are mild, it is natural to focus neuropsychological rehabilitation on the resources of the patients themselves. When the cognitive problems are more severe, the patient tends to be more dependent and neuropsychological rehabilitation should focus also on others' attitudes and PwMS environment.

Different components in neuropsychological rehabilitation

Giving information

One important component of neuropsychological rehabilitation is offering information about cognitive problems. In the beginning of the rehabilitation process it may be a good idea to discuss profoundly the results of neuropsychological assessment together with the patient. If needed, some additional neuropsychological tests can be performed to find out more precisely the problems the patient is having.

Goal setting

In the beginning of neuropsychological rehabilitation, the neuropsychologist and the patients should together set the goals for rehabilitation. It is useful to use as concrete strategies as possible, for example the SMART technique which is a part of goal setting procedure for example in the Goal Attainment Scailing (GAS) method (Kiresuk and Sherman, ). The family members of the patient should be with when setting the goal when possible.

Counselling, cognitive retraining, psychological support

An important part of neuropsychological rehabilitation is counselling. Counselling refers to a process where a neuropsychologist offers the patient information and guidance to support the patient to understand his/her cognitive strengths and weaknesses, the reasons for his/her cognitive symptoms and how to cope with the problems. The counselling is individually based and form a dialog where the patient has a possibility to reflect his/her situation and find ways to cope in the new situation. The main aim is to promote PwMS awareness, metacognitive skills and coping ability.

Cognitive retraining is an essential part of neuropsychological rehabilitation. Cognitive retraining aims at improving affected cognitive functions by training them either with paper and pencil techniques or with computerised retraining procedures. It seems that especially memory and attention retraining may improve MS patients' memory and attention functions. The ecological validity of this kind of rehabilitation is, however, not very high – the positive effects may be seen in the tasks similar to those retrained but may not have an effect on everyday functions.

Compensation consists of 4 elements:

- *Remediation*: direct training of a reduced function.
- *Substitution*: using other ways of achieving the same result
- *Accomodation*: adapt ones own goals and expectations to the present level of functioning (coping)
- *Assimilation*: adjust others expectations to the present level of functioning (inform significant others, care givers, society etc).

#### **4. COGNITIVE FUNCTIONS AND REHABILITATION OF DIFFERENT COGNITIVE DOMAINS /FOR THE NEUROPSYCHOLOGISTS AND PwMS**

##### **4.2 Memory**

Memory is the link between past and future, a system for registration, storage and retrieval of information. Memory informs our judgement, guides our behaviour, contributes to our personal identity. It influences our ability to learn new skills. Memory involves a number of different skills and stages. It can be likened to a music system in which cassettes and CDs are recorded and stored, and then retrieved from storage and replayed when required or to a filing system.

40 – 60% of PwMS report memory deficits. People with MS have particular difficulty with short term or recent memory, so are generally able to remember what happened a few days, weeks or years ago but may be unable to remember a conversation 15 minutes earlier or to go into a room for something and then forget why you are there. People without MS experience this type of difficulties too especially if they are distracted or tired, but for PwMS it is far more of a regular occurrence. The most common types of memory problems are difficulties in remembering recent events and remembering to carry out things. Some people with MS also say that it may take more time and effort to find the things to be remembered and to learn new things.

##### *Processes of Memory*

Attention – Attending to the information

Encoding – Taking it in

Storage – Putting in the right place

Consolidation – Rehearsing and practicing

Retrieval – Finding it and getting it back

##### *Different Types of Memory*

Can be divided into time periods involved (immediate; short-term; long-term and future) or type of information to be remembered (verbal; spatial; motor skill)

*Immediate or working memory:* this is the initial stage of memory where information is taken in through the senses where it is held for a very brief time usually a few seconds.

*Short-term memory:* Information that is stored just long enough to be used may be a few minutes, hours or days. Short-term memory enables to learn new tasks and new information. It can be separated into verbal and visual memory.

*Remote memory:* What people often refer to as their long-term memory. It is memory of past events, autobiographical memory and memory for public events and facts.

##### **4.2 Information processing**

People with MS find they often need more time to take in information and to make sense of it. It can also take them longer to formulate an appropriate response. Often PwMS report they have difficulties in processing sentences and this can be due to slowed processing. They might be finding a need a little extra processing time when having conversations. Also not only may they experience slowed processing but it is possible to experience attention and concentration problems (see attention section) and therefore you will be distractible. They may have to give greater effort to concentrate, and because their information processing speed may be slow, they take in less information. Therefore they may be thinking they have a memory problem. People with MS report an overall slowing in their speed of information processing of

visual information e.g. making sense of lots of road signs in a short distance, and auditory information e.g. following a set of verbal instructions or making sense of a conversation happening at normal speed. If a PwMS is experiencing slowed processing you will also be noticing you take longer to react to incoming information, this can cause a person to become frustrated.

### **4.3 Attention**

Attention is the cognitive process of selectively concentrating on one thing while ignoring other things. Attention and concentration form the basis for many other cognitive functions and are fundamental to learning and memory.

There are different aspects of attention, including:

- selective attention
- divided attention
- alternating attention
- sustained attention

#### *Selective Attention*

If patient tries to attend to one task over another then it requires selective attention. People with MS report they find it difficult to attend to more than one thing at the same time. They report difficulty in concentrating on one task and ignoring distractions.

#### *Divided Attention*

If patient tries to do two or more tasks at the same time then it requires divided attention. People with MS report difficulty in many situations requiring divided attention, for example, walking and talking, speaking on the telephone and writing down a message.

#### *Alternating Attention*

If the patient is trying to shift focus from one task to another, and back again, then it requires alternating attention.

#### *Sustained Attention*

If the patient is trying to concentrate on the same thing/task for prolonged periods require sustained attention. People with MS report they have difficulty in completing a task such as reading a book or watching TV as they find their “minds wander” on to other things meaning they have to reread the paragraph or ask what happened in the programme. Some people find it difficult to concentrate for long periods of time or have trouble keeping track of what they are doing when interrupted. It may also be difficult to do several jobs simultaneously or carry on a conversation while the TV or radio is on. Moreover, many people describe feeling as though they cannot function as quickly as usual.

### **4.4 Executive functions**

Executive functioning is the term used to describe the cognitive process that regulates a person’s ability to organise their thoughts and activities, to prioritise tasks, manage time efficiently, and to make decisions. Many people with MS experience at least some difficulties with executive functioning. They can experience difficulty in organising and prioritising thoughts, controlling expression of emotions and changing topics of thought. Some people experience difficulties when making plans and solving problems. People usually know what should be done but find it difficult to know where to begin or to work out steps involved in achieving their goals.

People with MS find they can experience difficulty in one or more of the following executive skills:

Planning and organising

Sequencing i.e. completing complex tasks in the right order.

Flexible thinking - they might find they are more rigid in their thinking, i.e. being inflexible and wanting to stick to fixed routines

Motivation/drive – some report an inability to start activities experiencing a lack of motivation or drive

Problem Solving

Self-monitoring

Self-correction

Distractibility

Diminished abstract reasoning – Poorer decision making

Executive functions and problem solving abilities seem to be especially vulnerable in MS related cognitive decline. Many people will experience mild problems yet their other cognitive processes, e.g. memory are not affected at all.

#### **4.5 Linguistic functions**

PwMS usually have relatively normal language function. However, at times you might notice some changes which can be quite frustrating. PwMS report they find difficulty with finding the word they are looking for this is best described as a “on the tip of your tongue” experience. They might know the word they want to use but just can’t get it out. They may notice you misname words, or may be able to describe the function of an item but not its actual. Some people with MS find difficulty with verbal fluency i.e. being able to choose the best words to express your feelings quickly. Sometimes people with MS start to answer a question and get sidetracked, talking about everything and anything without ever answering the question. At times they maybe aware of this and can find yourself asking “What was the question again?” People with MS may also experience difficulties in *finding the right word*. ‘It is on the tip of my tongue’ – you know the word but just cannot think of it.

#### **4.7 Visuoperceptual functions**

MS can affect the speed at which visual information is processed. Sometimes it is difficult for people with MS to make sense of what they see. Many PwMS report they can see the item, but it may not look like what they expected, or they struggle to make sense of what they see. “I am looking for my red t-shirt but can’t find it even though it is in front of me on top of the ironing pile”

PwMS report difficulty with angle matching, face recognition, judging depth and distance. E.g., walking into things such as doors, getting lost whilst driving even when you are familiar with a place – this may also be due to memory problems. Also may be problematic becoming confused over right and left directions, having trouble assembling things (e.g. toys; furniture) from diagrams or written instructions and having difficulty visualising objects from a verbal description

MS can also be related to other types of cognitive problems. However, deficits in language, visual perception or spatial relations are not so typical in MS.

#### **4.7 Alcohol and marihuana**

Some people think alcoho or marihuana helps their symptoms, such as tremor or bladder symptoms. Unfortunately both affect the central nervous system and can worsen MS cognitive symptoms. Using alcohol or marihuana or tobacco as a coping mechanism to deal with the troubles of MS may be tempting but can create more problems than it solves. Anger, frustration and relationship problems (particularly around caring) often lie behind heavy use of such drugs. Counselling or psychotherapy may facilitate less destructive ways of dealing with such feelings. It is important to drink sensibly – look at government guidelines and stick to them

Stronger forms of marihuana such as skunk, like alcohol, can have distressing long-term effects including

paranoia and severe loss of confidence as well as damage to the capacity to remember, to think and to make judgements. As such, they can increase the damage caused by the MS.

Relationships (including relationships between parents and children and between patients and professionals).can be severely impaired by alcohol or marihuana, since they reduce both motivation and capacity to take responsibility or to show concern for real problems as well as the capacity to care for others or the self. Alcohol and skunk can increase aggressivity; marihuana can increase passivity. Pwms sometimes report that they are more affected by alcohol than before diagnosis.

Alcohol can increase problems of loss of balance, uncoordinated movements, slurred speech and impaired judgement as well as damaging relations with others.

Carers may be pushed beyond the point where they can cope if they feel the pwms is increasing their problems by use of recreational drugs. Professionals may refuse treatment if a patient insists on smoking or is intoxicated.

## **Appendix 1**

### ***Computerized batteries***

#### **Rehacom**

**[www.hasomed.de](http://www.hasomed.de)**

RehaCom is a software package with which you can focus on the different cognitive areas you want to train. The system adapts the difficulty level to the patient's current performance level. All training results are saved. It has different modules to train attention, memory, executive functions, visual field and visuo-motoric coordination. Those modules are design to be used in neurological rehabilitation, geriatrics, psychiatry, pediatrics and multiple sclerosis. There is a study that evaluates its efficacy in people with MS. Purchasing licenses at home or on a network server is needed. English, German, French, Spanish, Italian, Portuguese, Russian, Dutch, Greek, Finnish, Norwegian, Swedish, Polish, Turkish, Estonian, Korean, Hebrew, Arabic, Chinese.

#### **CogniPlus**

**[www.schuhfried.com](http://www.schuhfried.com)**

*CogniPlus* is a cognitive training program. The *Aixtent* training programs led to the development of the *CogniPlus* attention training modules that are listed with recommendation strength A in the guidelines of the Society for Neuropsychology (Gesellschaft für Neuropsychologie - GNP, 2009) and the German Society for Neurology (Deutsche Gesellschaft für Neurologie – DGN, 2008). It also trains visual field (neglect), working memory, long-term memory, executive functions, spatial processing and visuo-motor skills. It identifies the client's ability level and adapts automatically to it. You can prepare and administer training sessions, manage client data and display training results. It can have different uses: children, geriatrics and as a neuropsychological rehabilitation tool. English, French, German, Dutch, Czech, Chinese, Arabic, Hungarian, Italian, Spanish, Polish, Portuguese, Russian, Slovak and Turkish.

#### **NeuroPsychOnline**

**[www.neuropsychonline.com](http://www.neuropsychonline.com)**

Website providing web based, clinical applications for the assessment, diagnosis and treatment of injury, disease or anomaly of the central nervous system. The *NeuroPsychOnline (NPO) Cognitive Rehabilitation Therapy System* consists of six Tracks of exercises designed to improve the user's cognitive skills (attention, executive functions, memory, visuospatial abilities, problem solving and communication). Each Track contains 12 Tasks (72 Tasks altogether), arranged in an order so that the most basic of cognitive skills are addressed first in therapy. As the user progresses, the Tasks evolve to become more complex and challenging. In addition, 69 of the Tasks contain four levels of difficulty and three contain three levels. *Softtools* and *Cognitive Enhancement Therapy* are developed using the same system. On-line, it requires subscription. English and Spanish.

#### **NeuronUp**

**[www.neuronup.com](http://www.neuronup.com)**

Web platform with materials addressed to neuro-rehabilitation professionals. It is designed to be used in the center. The professional plays an active role in developing the work plan. Lets you work with worksheets, games and simulators in order to train several cognitive functions (orientation, attention, language, memory, praxis, gnosis, visuospatial ability, executive function and social cognition), daily life activities (basic, instrumental and advanced) and social skills. No studies are available about its efficacy. On-line, it requires subscription. English, Spanish and Euskera.

## **Cognifit**

**[www.cognifit.com](http://www.cognifit.com)**

Oriented to general population as a general brain training tool that assess and stimulates different cognitive abilities (planning, auditory short-term memory, spatial perception, visual scanning, shifting, inhibition, visual short-term memory, eye-hand coordination, response time, working memory, contextual memory, naming, divided attention and updating). It changes according to the individual progress of the user. There is a study that evaluates its efficacy in people with MS. On-line. It's possible to train for free. English, Spanish, French, German, Italian, Brazilian, Portuguese, Dutch, Arabic and Japanese.

***Home-based personalized cognitive training in MS patients: a study of adherence and cognitive performance.*** Shatil E, Metzger A, Horvitz O, Miller A. *NeuroRehabilitation*. 2010;26(2):143-53

## **Brainworkshop**

**[www.brainworkshop.sourceforge.net](http://www.brainworkshop.sourceforge.net)**

Training of working memory through the Dual N-Back task. Only one activity that you can modify in order to change the difficulty. Provides daily progress graph. There are no studies of it's efficacy in people with multiple sclerosis. On-line free acces. English.

## **Lumosity**

**[www.lumosity.com](http://www.lumosity.com)**

Oriented to general population as a general brain training tool. It trains memory, attention, speed, flexibility and problem solving. Several studies evaluate it's efficacy but none in people with multiple sclerosis. On-line. It's possible to train for free but subscribing for a full access allow playing more games, a personalized training and get the training history. English.

## **Dakim**

**[www.dakim.com](http://www.dakim.com)**

Brain fitness software designed specifically for active adults over 60. It trains visuo-spatial orientation, short-term memory, long-term memory, computation, critical thinking and language and self-adjusts the challenge level. Available for home users, senior living communities and healthcare professionals. It has demonstrates its efficacy but not in people with multiple sclerosis. English.

## **Brain HQ**

**[www.positscience.com](http://www.positscience.com)**

*Brain HQ* is oriented to general population as a general brain training tool. It trains attention, brain speed, memory, people skills and intelligence. It has proven it's efficacy but not in people with multiple sclerosis. On-line, it requires subscription. English.

## ***MSQLI (Multiple Sclerosis Quality of Life Inventory)***

<http://www.nationalmssociety.org/ms-clinical-care-network/researchers/clinical-study-measures/msqli/index.aspx>

## **Appendix 2**

### **Strategies for PwMS**

#### **A2.1 Memory**

##### ***Methods to train memory for the specialists***

- The Story Memory Technique was based on the utilization of the visualization and logical context (e.g. story) in the learning and acquisition of new material
- to exploit memory notebooks systematically

##### ***Strategies to help as a recommendations for the PwMS – tips top improve memory***

Memory aids – Prompts, Post-it notes, Dry-wipe board, Notice boards, Calendars, Notebooks, Lists, Signs, Labels, Timers, Alarms, Watch alarms, Pill boxes, Key finders, Electronic Organisers, dictators, mobile phones etc. Etc.

##### **ASSOCIATION:**

Associate what you want to remember with what you know.

##### **VISUALISATION:**

Visualise a picture of what you want to remember. Consciously create an image in your mind of a task, number, a name, word or abstract thought.

##### **REMEMBERING IMPORTANT CONVERSATIONS**

Write down what people say – or use a Dictaphone

Keep a diary of important events or discussions

Write things down in an organised way

- Use headings
- Bullet points
- Underline
- Capital letters

##### **DIARIES**

Essential addition to anyone's memory whether for forward planning or for remembering past event – Powell (1994)

Page a day diary

Diaries entries can act as cues or triggers

Check diary regularly

- Cross out things you have done
- Write in future activities/events

## **A2.2 Information processing speed**

### **Methods to train information procession speed for the specialists**

#### **Strategies to help as a recommendations for the PwMS – information processing speed**

Try to avoid situations where you have to think on your feet

Give yourself permission to take more time

Break information into small steps

Turn off distractions like TV/radio/mobile phone

Try to avoid over-stimulating environment

Have patience

Set yourself small achievable goals and practice tasks as this will help your speed. Brain training is helpful for this

Use positive self-talk – acknowledge to yourself that you are not mad, stupid, lazy, useless, crazy or nuts. Say to yourself “I know I can do this when I have a little more time

Be brave and tell others what you need maybe ask them to “say that a little slower please”, “please repeat what you said”

Allow more preparation time. Think about the points you need to get across and the points you need clarified for yourself. Write them down beforehand and re-read them. Refer to the notes as the conversation progresses

Organise tasks that require more energy for when you know you are not fatigued i.e. the best time of day for you

Take notes of conversations, either during the conversation, or immediately after video or download television programmes you want to discuss with others, and watch them again

## **A 2.2 Attention**

### ***Strategies to help as a recommendations for the PwMS – tips to improve attention***

#### Paper-pencil tasks

- simple scanning tasks (with and without distracters) to exercise basic attention
- tasks requiring divided attention (making two or more things at the same time) – first exercising accuracy, then speed

#### Computer-based training

- several computer-based training programs (for example Vienna Test system etc)
- In Finland we use the attention module of the Foramen rehabilitation program (which consists of several different tasks with variable difficulty on different areas of attention)

#### If you find it difficult to concentrate for longer periods:

- try to take the effects of tiredness and fatigue into account
- plan activities so that you do your most demanding work at your best times.
- try not to place big demands on your concentration when you are feeling tired.
- Pace yourself.
- Schedule rest periods.
- Use relaxation techniques.

#### If you lose track of what you are doing if you are interrupted:

- Try to reduce the number of distractions when you are talking to someone or working on a particular task.
- Turn the TV or radio off, and do one thing at a time.
- Try to work in a private room, so there are few distractions.
- Put the telephone onto voicemail or use the answer-phone while you are dealing with a task, so you are not constantly interrupted.

## **A 2.3 Executive functions**

### ***Strategies to help as a recommendations for the PwMS – executive functions***

Step back. If you are struggling with a task take a step back, don't rush in and think about it for a few moments before starting.

Set specific goal for specific times/days

Schedule activities – use calendars, electronic devices, computers to help you plan and schedule activities

If it is a problem to plan meals and you tend to be impulsive i.e. make you mind up on the day running to the shop to see what you could have for tea, try write up a meal plan for the coming week. Go through the recipes and check the ingredients you need on your shopping list.

Be kind to yourself and reward yourself for achieving a task

Sequencing - Make a list of steps needed to achieve the task. If necessary simplify the task by breaking it down into small steps, and write these down then follow the steps in the correct order crossing out each step as you complete it.

Make checklists of the tasks you struggle with using the sequencing strategy mentioned above. Laminate these checklists and then use a white board marker to cross steps off. At the end of the task you can wipe the marks off and use again another day. Ideas for checklists might include things like programming the DVD player or video, using the internet etc. If you struggle to think of the order of steps ask someone to help you in sequencing/ordering the task

When you are struggling to solve problems work through your problems with someone you trust. It might help to write down the problem you are struggling with first and when you discuss it with your friends write down their alternative solutions as soon as they mention them

If you are making frequent errors take a step back and look at the task see if you can recognise the errors and then try do the task differently. Try to be flexible by looking at the problem from a different angle. Give yourself permission to take longer to do the task. If you are struggling with this ask someone else to help you

Each day write out the jobs you would like to achieve, number them in order of priority, so you start with the most important ones. If you don't complete them all write a "carry over" list for the next day – reminding yourself this is ok and you are not a failure.

If you are struggling with your finances try using a budget book to track money spent. Some have columns of alternating shading, so are easier to use, as they provide more visual clues. Or you may like to use a computer generated spread sheet for budgeting and financial record keeping

If family/friends tell you there is a problem try to be calm and ask for support in working out the difficulty.

## **A2.4 Linguistic functions**

### ***Methods to train linguistic functions for the specialists***

#### ***Strategies to help as a recommendations for the PwMS – linguistic functions***

Encourage people you know not to tell you the word you are finding it hard to say

Self-cueing

- Using the first letter of a word
- Going through different categories and sub-categories

Talking around the subject

- Describe it
- Talk around it
- Don't get hung up on finding the right word
- Getting the message across it what is important

Use gestures

Try getting a picture in your mind of the object, person or idea you want to retrieve

Write down words on post-it notes

If you lose your train of thought, take 2 or 3 deep breaths and start again or use the strategy of getting a picture in your mind to help you

Try chunking information – put like ideas together

Use key words to organise thoughts before sitting down to write

Be patient

## **A2.5 Visual perception**

### ***Methods to train visual perception for the specialists***

### ***Strategies to help as a recommendations for the PwMS – visual perception and spatial difficulties***

If you keep walking into doors – Put tram lines of tape on the floor to walk between

If you find you are forgetting passages or missing the end of sentences when reading – Use a piece of paper to cover text and guide reading

Reduce clutter

Keep things in consistent places

Increase contrast

- Scanning
- Dark objects on white background or vice versa
- Coloured tape on sharp corners

Use written and visual cues

Get your eyes checked – you might be having problems because you need glasses.