The Role of Neuropsychology in the Treatment of MS

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QOL = quality of life.

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Spectrum of Neuropsychology

Personality

Mood

Behavior

QOL, social function

Language

Memory

Attention

Executive function

Visuospatial abilities

QOL = quality of life.

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Impact of Inflammatory Damage

- Physical and/or Sensory Symptoms
- Neuropsychological Symptoms

Neuropsychological Dysfunction in MS
Indicators of Potential Neuropsychological Dysfunction in MS

◆ “I am slower in my thinking - I get it but it takes longer.”

◆ “I need to make lists more often.”

◆ “I need more help in managing my finances.”

◆ “I can’t remember where I put my keys.”

Indicators of Potential Neuropsychological Dysfunction in MS

◆ “I can’t do two things at once.”

◆ “I can’t seem to find the right words.”

◆ “My mood is up and down several times daily.”

◆ “I cry more easily.”

◆ “I am not as interested in people as I was.”
Indicators of Potential Neuropsychological Dysfunction in MS

- Help in ADLs in the absence of disability.
- Unemployment in the absence of physical disability
- Mood disorder other than depression
- Withdrawal from usual activities/socialization
- Opinion of significant other personality shift

Natural History of Cognitive Impairment in MS

- Prevalence is 45-65%
- Pattern and degree of involvement is variable
Neuropsychological Dysfunction in MS

COGNITIVE domains regularly affected:
- Attention
- Learning and Retrieval (Memory)
- Information processing speed
- Visuospatial perception
- Executive Function

COGNITIVE domains usually spared:
- Language/Verbal Skills

Paced Auditory Serial Addition Test (PASAT)

Percent Correct

Control
Multiple Sclerosis

Easy (3s) Hard (2s)

4 6 3 1 9 5
“10” “9” “4” “10” “14”
Neuropsychological Dysfunction in MS

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Components of Memory

ENCODING
(getting the information in)

CONSOLIDATION
(transferring the information into long-term store)

RETRIEVAL
(getting the information out)

Free Recall vs. Recognition Memory
Neuropsychological Dysfunction in MS

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Neuropsychological Dysfunction in MS

- Associated with:
  - Increased unemployment (16% vs 44%)
  - Decreased ADLs
  - Decreased socialization
  - Psychopathology

The Impact of Cognitive Dysfunction On Daily Living

“Limitations in a patient’s work and social activities are correlated with the extent of cognitive decline, independent of degree of physical disability.”


How accurate is a person with MS about his/her cognition?

- Patient’s perception of overall cognitive functioning is not consistent with performance on cognitive tests
- Depression, anxiety, fatigue, and level of disability predict patient perception of cognitive functioning. Actual test performance does not.

What medical and non-medical techniques can you use if you have cognitive difficulties?

First, we need to know exactly what the problems are (or even if there really are any)....

Assessment Of Cognitive Dysfunction

- **MS Functional Composite** (NMSS Clinical Outcomes Assessment Task Force, 1997)
  - 3 measures (includes PASAT)
  - used as outcome measure in clinical trials,
  - administered and scored by non-neuropsychologist
MS Functional Composite

- Timed 25 Foot Walk
- 9 Hole Peg Test
  - average of right and left arms
- Paced Auditory Serial Addition Test
  - number correct, 3 sec. version

Assessment Of Cognitive Dysfunction

- Neuropsychological Screening Battery (Rao et al., 1991)
  - 20-30 minutes to administer, used to screen patients in clinical setting
  - administered and scored by non-neuropsychologist
- MACFIMS (Benedict et al., 2003)
Assessment Of Cognitive Dysfunction

- **Comprehensive Neuropsychological Examination**
  - 3-5 hours, addresses differential diagnosis, disability questions
  - administered/interpreted by clinical neuropsychologist
  - Should expect full report with conclusions (e.g., MS or depression) as well as recommendations (for work, school, etc).
  - **REIMBURSEMENT IS MORE FREQUENT THAN MIGHT BE BELIEVED. NEEDS TO BE A MEDICAL DIAGNOSIS (340, MS) AND A CPT CODE FOR NEUROPSYCHOLOGICAL TESTING (96117) BILLED BY A NEUROPSYCHOLOGIST. SOMETIMES, PRE-CERT NEEDED.**

- **Computerized Screening Battery** (Wilken et al., 2003)
  - 25-30 minutes to administer
  - administered and scored by non-neuropsychologist
  - Interpreted by neuropsychologist
  - correlates highly with traditional measures

Next, we can address your individual weaknesses

COGNITIVE domains regularly affected:

- Attention
- Learning and Retrieval (Memory)
- Information processing speed
- Visuospatial perception
- Executive Function

Strategies to help with attention problems

- Breaks
- Multi-tasking
- Location of workspace
- Organization of workspace
- Sleep hygiene
- School- location of desk
Neuropsychological Dysfunction in MS

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Components of Memory

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RETRIEVAL
(getting the information out)

Free Recall vs. Recognition Memory
Strategies to help with memory problems

- Organization of new information
- Format of new information (e.g., verbal, visual)
- Mnemonic techniques
- Be sure attention is good when learning (see prior slide on attention)
- Cues during learning and recall
- Recording meetings/classes
- Notetaking service in school
- Modality dependent learning
- Do what you can to minimize fatigue (sleep hygiene, breaks)

Neuropsychological Dysfunction in MS

COGNITIVE domains regularly affected:

- Attention
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- Information processing speed
- Visuospatial perception
- Executive Function
Strategies to help with slowed information processing speed

- One task at a time
- Seek out work that allows you to go at own pace
- Seek out accommodations at work and school
- Record information (tape, digital recording device)
- Note-taking service
- Voice activated computer software
- Do what you can to minimize fatigue (sleep hygiene, breaks)

Neuropsychological Dysfunction in MS

COGNITIVE domains regularly affected:

- Attention
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- Executive Function
Strategies to help with perceptual difficulties

- Be sure to have eye exam to rule out non-MS visual problems
- Request written directions instead of maps
- Request written instructions instead of flow charts
- If you drive, keep it to daytime and on familiar roads
- When learning new information, try to learn it aurally

Neuropsychological Dysfunction in MS

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Symptomatic Treatment: Cognitive Rehabilitation

- Direct training in compensatory strategies (neuropsychological treatment) associated with improved visuospatial memory, decreased depression (Jonsson et al., 1993)
- Training in attention associated with improved attention performance for at least 9 weeks (Plohmann et al., 1997)
- Neuropsychological training (education, social skills training, behavioral modification) showed improvement of social behavior (e.g., egocentric speech) (Benedict et al., 2000)
- Cognitive therapy led to improved verbal learning, verbal abstraction, and depression (Rodger et al., 1996)

Brain plasticity in MS

- Patients with mild cognitive impairment recruit additional functional areas
- Functional integration of frontal and parietal association areas seems to allow for cognitive compensation

(Penner et al., JNeurol, 2003)
What does neurocognitive retraining mean?

- **Term** of neurocognitive retraining in the sense of a neuroscientific method
  - created in the nineties when brain imaging techniques came in the focus
  - focus of interest on specific brain functions and their interaction
  - development of more sensitive neurocognitive tools to differentiate brain functions
  - application of tools in the normal and the injured brain

- **Rationale**
  - to identify those cognitive functions that are mainly affected in a patient (e.g. attention, memory, executive functions)
  - to compose a training tool for these cognitive functions
  - to stimulate alternative pathways by training (“unmasking” of latent pathways in the sense of Parry et al., 2003)
    - neurocognitive retraining as an intervention that is targeted on changes in specific neuronal circuits
  - to improve cognitive functioning
  - to transfer improvement into normal daily life
How useful is neurocognitive retraining?

- The study by Jønsson et al. (1993)
  - 40 MS patients
  - Neuropsychological testing at baseline, assessment of depression and anxiety Allocation to one of two groups
    1. Specific cognitive treatment (neuropsychotherapy and cognitive training)
    2. Non-specific mental stimulation (diffuse: discussion of films, newspaper articles, playing games)
  - Treatment lasted 1 to 1.5 hours 3 times a week
  - After 45.6 days first retest (short-term effects of treatment). After 6 months second retest (long-term effects of treatment)
  - Result: Moderate benefit of specific cognitive treatment with the most significant effect on depression in the specific treated group

- The study by Plohmann et al. (1998)
  - 22 MS patients
  - Computerized test-battery for attention functions (TAP; Zimmermann & Fimm, 1992)
  - Computerized training on two of the most impaired functions by AIXTENT (Sturm et al., 1993)
  - Training was applied consecutively resulting in a design where one function was trained specifically and the other in a non-specific manner
  - Training lasted 40 min over 3 weeks including 12 sessions
  - Results: Significant improvements of performance primarily due to specific cognitive training
How useful is neurocognitive retraining?

The study by Solari et al. (2004)

- 82 MS patients
- Randomized double-blind, controlled trial
- BRB-N (Rao, 1990)
  - Assignment to two computer-assisted retraining interventions by RehaCom (www.Schuhfried.at)
    - 1. Memory and attention (study arm)
    - 2. Visuo-constructional/visuo-motor coordination (control arm)
- Training included 16 training sessions over 8 weeks, each training lasting 45 minutes, twice a week
- Results: Benefit of cognitive treatment on primary outcome measure BRB-N, but specificity does not account for it

How useful is neurocognitive retraining?

The study by Müller et al. (in prep.)

- Results:
  - No significant differences between a specific, computerized attentional training and traditional general occupational training
  - Training responses of individual attentional sub-functions were inversely related to the prevalence of impairment in this population
    - The most commonly impaired attentional sub-function speed was most resistant to training. Less frequently impaired sub-function accuracy was most responsive
  - Cognitive training appeared particularly effective in patients with the greatest impairments
- Conclusions: A targeted training of cognitive functions with methods of “guided recovery” should be considered for patients with impairments in accuracy while training for patients with predominant slowing should focus on compensatory cognitive, emotional and social strategies
Cognitive Retraining: the future

- The positive results found in several studies should motivate to go on with cognitive retraining studies.
- But: problems with existing cognitive retraining studies:
  - small sample sizes
  - heterogeneous MS samples with respect to
    - disease course
    - disease duration
    - EDSS
    - degree of cognitive impairment
  - heterogeneous cognitive outcome measures
    - benefit for daily life
    - cognitive test measures
  - no definition of optimal time intervals
  - insufficient study designs with respect to
    - blinding
    - controls

Impact of Psychiatric Factors on Cognitive Functioning

MOOD disorders:

Anxiety, depression, mania, usually accompanied by neuro-vegetative symptoms as well as negative patterns of thought and behavior.
Mood Disorder in MS

DEPRESSION

- Incidence significantly increased over non-MS population
- Possible MRI correlate: Frontal lobe lesions

Some Signs of Depression

- Decreased energy & increased fatigue.
- Feelings of worthlessness, guilt & self-reproach.
- Indecisiveness, memory loss, difficulty in concentrating. Depressed MS patients perform worse than non-depressed MS patients on measures of cognition (Arnett et al., 1999)
- Irritability, short temper or rage.
Mood Disorder in MS

BIPOLAR Disorder:

- Incidence 2-13% of MS patients
- Familial clustering of bipolar disorder and MS reported

EMOTIONAL DYSREGULATION

- Pathologic laughing and crying: May be a “disconnection” or “imbalance” of perceived and displayed emotions
- Localization: Unknown: Thalamic-Hemispheric disconnection?
- Prevalence: Unknown. No scales

STRESS

- Stress is a fundamental component of life. It is an unconscious response to a demand and when the demand is perceived as excessive, stress results along with diseases and conditions.

- We almost never have control of the demand...

Stress

- But we do have control over our response to that demand.

- Importantly, the demand itself can be very positive (the holidays, getting married, receiving a promotion, etc.)
Fight or Flight Response

- This fundamental physiologic response forms the foundation of modern day stress medicine.
- The "fight or flight response" is our body's primitive, automatic, inborn response that prepares the body to "fight" or "flee" from perceived attack, harm or threat to our survival.

Psychoneuroimmunology (PNI)

- *Psychoneuroimmunology (PNI)* has given importance to the relationship between stress and its physiological effects on the body.
- Scientists in this growing field have discovered that stress modulates the activities of the nervous, endocrine, and immune systems.
WHAT WE KNOW

Stress negatively impacts MS, and can trigger MS exacerbations…

STRESS and MS

- Diagnostic uncertainties.
- MS is unpredictable.
- Invisible symptoms (e.g. cognitive speed)
- Visible symptoms (e.g. gait disturbance)
EVERYONE EXPERIENCES MS SYMPTOMS DIFFERENTLY

- UNPREDICTABILITY
- Reduced control

* These are the hallmark psychological components of stress

STRESS

- Stress alone does not necessarily determine how well or poorly the immune system will function.
- The important factor is the individual’s ability to cope with stress (Blauer-Wu, 2002).
- How an individual perceives and responds to stressful event may be more important than the existence of the stress itself.
STRESS

- Individuals with high stress levels and excellent coping skills may have minimal effects on the functioning of their immune systems.

- A low level of stress in individuals who have poor coping skills may have significant alterations in their immune functioning.

What is the impact of stress on memory?

Cognitive:

- Poor memory.
- Inability to concentrate.
- Reduced ability to multi-task.
Immediate results of Negative Stress

Mental

- Poor memory.
- Inability to concentrate.
- Low levels of creativity.
- Poor self-control.
- Low self-esteem.

What can be done about stress and depression

Exercise

- Stretching
- Yoga
- Massage
- Healthy, well balanced diet
- Sleep hygiene
- Counseling
Stress Management Strategies

- Relaxation
- Deep breathing, progressive muscle relaxation, visualization, meditation, autogenic relaxation.
- Bath, reading, nature, leisure activities
- Talking to others, utilizing social supports
- Laughter
- Crying

The Bottom Line:

- The actual amount of stress is not as important for determining its effect on the immune system as an individual’s coping skills.

- Treatment of stress (and other psychological issues) is essential in the management of MS-related cognitive problems and the general health of MS patients.
Neuropsychological Evaluation can assess cognition and psychological functioning. This can guide treatment and assist with respect to:

- Accommodations as per ADA
- Compensatory Strategies
- Differential Diagnosis (i.e., MS versus Depression/Anxiety)
- Obtaining services (e.g., cognitive rehab, psych treatment)

Conclusions

- MS causes cognitive problems in 45-65% of MS patients. These cognitive problems can negatively affect mood, functioning, and quality of life, and there are things we can do to address them.

- Mood, Stress, and Psychological Well-being matter!

- Neuropsychologists play a large part in assessing cognitive and psychological functioning, and we can help to guide treatment for these issues.