COGNITIVE AND BRAIN CHANGES IN MULTIPLE SCLEROSIS

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Objectives

1. Identify cognitive challenges in multiple sclerosis and their measurement.
2. Understand the importance of brain and cognitive reserves.
3. Learn about how to keep and build active minds and healthy brains.
Overview

• Brain & Cognition in MS
• Measuring Cognitive Challenges in MS
• Brain/Cognitive Reserve
• What To Do
Overview

• Brain & Cognition in MS
  • Measuring Cognitive Challenges in MS
  • Brain/Cognitive Reserve
  • What To Do
Brain changes in MS

• In MS, the immune system mistakenly attacks and damages the central nervous system (CNS).
Brain changes in MS

- Damage to the brain’s white matter slows information throughput.

By Dr. Jana - http://docjana.com/#/saltatory
Brain changes in MS

- In addition to lesions, there is brain tissue loss (atrophy).
- If MS is left untreated, tissue loss is faster and more pronounced in pwMS (~ premature “brain aging”).
Cognition and brain changes in MS

Most of the brain changes observed in MS relate to changes in cognitive functions.

In particular:

- Thalamus
- Hippocampus
- Pre-frontal/ frontal cortex
- Connections between these
Thalamus & cognition in MS
Almost all sensory information passes through the thalamus.
Thalamus & cognition

Thalamus & cognition

Overview

• Brain & Cognition in MS

• Measuring Cognitive Challenges in MS

• Brain/Cognitive Reserve

• What To Do
Cognitive challenges in MS

Information Processing Speed

Learning and Memory

Attention

Executive Functions

Language

Spatial

Any cognitive challenge: 40% - 70% of pwMS
Cognitive functions

- **Information processing speed**
  - How fast (sensory) information is passed on and evaluated

- **Learning and Memory**
  - Learning: Acquiring and storing new information
  - Memory: Retrieving stored information

- **Attention**
  - Divided: Concentrating one two (or more) things at once
  - Selective: Concentrating on one thing, ignoring others

- **Executive functions**
  - Umbrella term: Cognitive flexibility, planning, prioritizing
  - Orchestrating the other cognitive functions
Cognitive functions

• **Language**
  • Production, comprehension, reading

• **Visuo-spatial functions**
  • Visual perception & construction, navigation

Less or unaffected
Cognitive challenges in MS

• Can go unnoticed and/or are attributed to depression, fatigue, or stress.
• Are only weakly related to other disease characteristics and disability (motor ≠ cognitive).
• Can occur at any time, but are more common later in the disease.
• Possible in any disease course, but are more likely in progressive MS.
MS is not dementia

- Cognitive challenges in MS are usually milder than in dementia, like in Alzheimer’s Disease.
- The progression of cognitive deficits is also less severe in MS than in AD.
- There is no evidence that the risk for getting AD is higher in pwMS.
- The biology of the two conditions is different.
- Largely unsuccessful intervention studies with AD medications (like donepezil) in MS.
Measuring cognition

**REPORT**

- Subjective report of cognitive issues.


15 questions for pwMS & informant.

But the MSNQ also reflects mood.
Measuring cognition

**REPORT**

- Subjective report of cognitive issues.

**NEUROPSYCHOLOGICAL TESTING**

- Objective assessment of cognitive functions with standardized and normed test instruments.
Neuropsychological testing

- Full examination
- Neuropsychological screening

Neuropsychological tests are:

Standardized: Applied in the same way.
Normed: Healthy people’s performance is known.
Neuropsychological examination

• Has to be led by a clinical neuropsychologist.

• Usually guided by a specific question (like “Can I drive a car safely?”).

• 1-3 hours, sometimes several sessions.
Neuropsychological screening batteries

- Minimal Assessment of Cognitive Function in MS (MACFIMS)
- 7 tests (90 min.)

MACFIMS: Benedict et al. 2002; *Clinical Neuropsychologist*, 16, 381–397

- Processing speed/working memory
- Learning and memory
- Executive function
- Visual-spatial processing
- Verbal fluency
Neuropsychological screening batteries

• Brief Repeatable Battery of Neuropsychological Tests (BRB-NT)
  • 5 tests (30 min.)


Processing speed/working memory
Learning and memory
Verbal fluency
Neuropsychological screening batteries

BICAMS (Brief International Cognitive Assessment for MS) is an international initiative to recommend and support a cognitive assessment that is brief, practical and universal.

- Symbol-Digit Modalities Test
- CVLT-2
- BVMT-R

Benedict et al. (2012) BMC Neurology, 12, 55
Neuropsychological screening batteries

BICAMS (Brief International Cognitive Assessment for MS) is an international initiative to recommend and support a cognitive assessment that is brief, practical and universal.

- Symbol-Digit Modalities Test
- CVLT-2
- BVMT-R

~ 15 min.
Material: Paper, pen, stopwatch
Initial expert training

Benedict et al. (2012) BMC Neurology, 12, 55
## Symbol Digit Modalities Test

### Faux Example

<table>
<thead>
<tr>
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Symbol Digit Modalities Test

Faux Example

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Outcome: Number of correct responses in 90 seconds
## CVLT-2

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<th>Faux Example</th>
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<tbody>
<tr>
<td><strong>Apple</strong></td>
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<td><strong>Tiger</strong></td>
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<td><strong>Boat</strong></td>
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<td><strong>Airplane</strong></td>
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### CVLT-2

**Faux Example**

<table>
<thead>
<tr>
<th>6 / 16</th>
<th>Boat</th>
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<th>Car</th>
<th>Lion</th>
<th>Leopard</th>
<th>Apple</th>
<th>Shoes</th>
<th>Airplane</th>
<th>Puma</th>
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<th>Gloves</th>
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# CVLT-2

Faux Example

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<td>6</td>
<td>16</td>
<td>8</td>
<td>16</td>
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</table>

Outcome: Number of correct responses across five learning trials
BVMT-R

Faux Example
BVMT-R

Faux Example
BVMTR

Faux Example

2 points

0 points

1 point

Benedict et al. BMC Neurology 2012, 12:55
BVMT-R

Faux Example

Outcome: Total score across 3 learning trials

Benedict et al. BMC Neurology 2012, 12:55
Canadian outcomes

Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS): Canadian contribution to the international validation project

Lisa A.S. Walker a,b,c,d,e,f,* , Leila Osman a,g , Jason A. Berard b,d , Laura M. Rees a,b,d,e , Mark S. Freedman a,b,c , Heather MacLean a,b,c , Denis Cousineau d

a University of Ottawa Brain and Mind Research Institute, Canada
b The Ottawa Hospital Research Institute, Canada
c University of Ottawa, Faculty of Medicine, Canada
d University of Ottawa, School of Psychology, Canada
e Carleton University, Department of Psychology, Canada
f Carleton University, Institute of Cognitive Science, Canada
g St. Paul University, Canada
Main outcomes: BICAMS Canada

• 51 pwMS, 57 healthy controls
• At least 1 test impaired: 58% of pwMS
• Most sensitive: SDMT
• Related to employment status: BVMT-R
• Some practice effects → newly emerging impairment meaningful

• Walker et al. (2016): Canadian norms and cut-off scores
Summary 1

- Cognitive challenges are common in MS and related to brain changes.
- Processing speed and learning/memory are most affected.
- MS is not dementia.
- Neuropsychological testing or screening is needed:
  - to know if cognition is compromised
  - to know if cognition changes over time
- The BICAMS is an easy-to administer screening, and now also has data from Canada.
Overview

- Brain & Cognition in MS
- Measuring Cognitive Challenges in MS
- **Brain/Cognitive Reserve**
- What To Do
Brain Reserve & Cognitive Reserve

• *Hardware vs. Software*

• Brain reserve: ‘More brain tissue’ is a buffer to delay the onset of noticeable cognitive problems.

• Cognitive reserve: Having many ways to do a cognitive task makes it more robust to brain damage.
Reserve in MS

• In MS: Ongoing noticeable (e.g., relapses) and less noticeable damage can reduce brain reserve.

• Within limits, the brain adapts to these changes and compensates for lost function → Plasticity.

• If there is no more reserve, compensation becomes impossible.

→ Important to protect reserve.
Brain Plasticity in MS

• How does brain function change under neurological challenges like in MS?
Brain Plasticity in MS

• How does brain function change under neurological challenges like in MS?

• To compensate, damaged brain structures may have to communicate more to each other

→ Increased “functional connectivity”
Brain Plasticity in MS

Thalamus (and insula): Increased functional connectivity

→ the brain has to “work harder”
→ fatigue!


Brain plasticity in relapsing–remitting multiple sclerosis: Evidence from resting-state fMRI
http://dx.doi.org/10.1016/j.jns.2011.01.023
Brain Structure, Function & Cognition

Hypothetical relationship between the 3 over time

Brain Reserve & Cognitive Reserve

• *Hardware vs. Software*

• Brain reserve: ‘More brain tissue’ is a buffer to delay the onset of noticeable cognitive problems.

• Cognitive reserve: Having many ways to do a cognitive task makes it more robust to brain damage.
Cognitive Reserve & MS

“Enrichment” — Education, but also leisure activities, hobbies, social activities, etc.
Summary 2

• Brain and cognitive reserves protect against cognitive decline in MS.
• The brain is ‘neuroplastic’, also in MS.
• Compensates for some of the lost tissue.
• Compensation requires energy.
• Compensation is less likely when reserves are smaller.
Overview

• Brain & Cognition in MS
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• Brain/Cognitive Reserve

• What To Do
Keeping and building reserves

Goal

• Keep your brain healthy
• Keep your mind active
• ...and your body, too
Treating cognitive challenges in MS

- **Pharmacological**
- Disease-modifying medications in relapsing MS.
- Mixed or null findings for progressive MS and for other drugs.
- Promising: Amphetamine (trials ongoing; Dr. S. Morrow, London, Ont.)
- Alternatives are urgently needed.
Treating cognitive challenges in MS

- Cognitive Rehabilitation

- MEMREHAB trial
  Intervention: Story Memory Technique
  → Memorizing words by creating visuals and story context.
  → 1 h sessions, 2 x week over 5 weeks

Cognitive Rehabilitation

- Learning (CVLT) improved for the intervention group.
Cognitive Rehabilitation

- Learning (CVLT) improved for the intervention group.
- The intervention also made everyday memory better transfer
Cognitive rehabilitation

• Learning (CVLT) improved for the intervention group.

• The intervention also made everyday memory better → transfer

• ...and the memory boost was still there after 6 months.

Cognitive rehabilitation

• But: The intervention was less effective in pwMS with additional processing speed slowing (Chiaravalloti, N. D., & DeLuca, J. (2015). *Multiple Sclerosis Journal, 21*(12), 1575-1582).

• Other cognitive rehabilitation studies had more mixed findings.
Cognitive rehabilitation

• We need more research to find out:
  • who benefits most from
  • which type of cognitive rehab, and
  • how much is needed (“dosage”)


Strategies (http://www.nationalmssociety.org)

Restorative

- Combine modes of learning
- Repeat & verify
- Spaced rehearsal
- Build associations
Combine modes of learning

Hi, my name is Anna.
Combine modes of learning

Hi, Anna.
Combine modes of learning
Combine modes of learning
Build associations

Grandma Anna
Build associations
Imagery
Strategies (http://www.nationalmssociety.org)

Compensatory

• Consolidate and centralize
• Plan
• Record
• Remind
• No distractions
• Take a break
• Do one thing at a time
Role of physical activity

- Several studies now suggest physical activity improves cognition (and other symptoms) in MS.
Role of physical activity

• Several studies now suggest physical activity improves cognition (and other symptoms) in MS.
• **Aerobic** (aka cardio-) exercise in particular.
• Even some recent evidence for brain changes!
Role of physical activity

Exercise training effects on memory and hippocampal viscoelasticity in multiple sclerosis: a novel application of magnetic resonance elastography

Brian M. Sandroff¹ · Curtis L. Johnson² · Robert W. Mott³

Aerobic exercise increases hippocampal volume and improves memory in multiple sclerosis: Preliminary findings

V. M. Leavitt¹,², C. Cirnigliaro³,⁴, A. Cohen¹, A. Farag³, M. Brooks³, J. M. Wecht³, G. R. Wylie¹,², N. D. Chiaravalloti¹,², J. DeLuca¹,², and J. F. Sumowski¹,²

¹Kessler Foundation Research Center, West Orange, NJ, USA
²Rutgers – New Jersey Medical School, Newark, NJ, USA
³James J. Peters VA Medical Center, Bronx, NY, USA
⁴Kessler Institute of Rehabilitation, West Orange, NJ, USA
Key study outcomes

- Small studies, including pw RR-MS.
- Aerobic exercise over 12 weeks of progressive treadmill walking or stationary cycling exercise (3x weekly).
- Improvement in memory and learning
- Increased volume of the hippocampus
- Reduced ‘elasticity’ of the hippocampus
Role of physical activity

Effects of exercise on fitness and cognition in progressive MS: a randomized, controlled pilot trial

S Briken¹,², SM Gold¹, S Patra³, E Vettorazzi⁴, D Harbs³, A Tallner⁵, G Ketels⁶, KH Schulz³,⁷ and C Heesen¹,²
Key study features

Study
- People with progressive MS (EDSS 4–6).
- 3 different aerobic exercise groups
- 8-10 weeks duration

Outcome measures
- Cognition
- Aerobic fitness
- Walking
- Fatigue
- Depression
Aerobic exercise interventions

Rowing ergometer

Arm ergometer

Bicycle ergometer
Memory outcome

Better memory in all intervention groups

Summary: What to-do

• Keep mentally active
• Continue leisure activities
• Use strategies to help you focus and remember things
  • “Information central”
  • Enrich your learning (associations, multiple modes)
  • Use reminders
  • etc.
• Try or continue a cardio-exercise
Review article

Brain health: time matters in multiple sclerosis

Gavin Giovannoni a,*, Helmut Butzkueven b, Suhayl Dhib-Jalbut c, Jeremy Hobart d, Gisela Kobelt e, George Pepper f, Maria Pia Sormani g, Christoph Thalheim h, Anthony Traboulsee i, Timothy Vollmer j

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Thank you