

Cognitive dysfunction in multiple sclerosis

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Aims

1. How common is cognitive dysfunction?
2. What is cognitive dysfunction?
3. How can cognitive dysfunction be detected?
4. How can cognitive dysfunction be treated?



PHOTOGRAPHIE

des CHAMPS ELYSEES

à Mr. le D^r Freud. Souvenir de l'admission
1886. 24 jours

How common is cognitive dysfunction in MS

prevalence rates

- Community samples
 - 40% (Rao et al, 1991)
 - 46% (McIntosh-Michaelis, 1991)
- Tertiary clinics
 - 50-60% (Benedict et al, 2006)

Cognitive dysfunction in MS:

Clinical significance

- Cognitively impaired MS patients may experience greater difficulties with respect to work, relationships, vocational functions, sexual function and activities of daily living.

What is cognitive dysfunction?

- **Reduction in cognitive speed**
- **slowness in information processing**
- Memory impairments
- deficits in abstracting
- attention and vigilance impaired
- language largely spared

**How can cognitive dysfunction
be detected?**

Assessing cognition

self report

- Multiple sclerosis neuropsychological questionnaire (MSNQ)
- 15 questions for patient
- 15 questions for informant
- Informant responses more accurate reflection of patient's cognition
- Patient complaints of impaired cognition may better reflect depression.

Screening batteries

- Brief Repeatable Neuropsychological Battery
 - 15 alternative, equivalent versions
 - Consistent Long Term Retrieval (Selective Reminding Test)
 - 10/36 Spatial Recall Test
 - COWAT
 - PASAT
 - SDMT

Brief Repeatable Battery of Neuropsychological Tests (BRB-N)

Verbal
Memory

Selective Reminding
Test

Visuospatial
Memory

10/36 Spatial Recall
Test

Verbal
Fluency

Controlled Oral Word
Associated Test

Processing
Speed

Symbol Digit Modality
Test

Sustained
Attention

Paced Auditory Serial
Addition Test

- Duration: ~ 30 min.
- Most widely used
- 15 alternate forms for serial testing
- Sensitivity: 71%
- Specificity: 94%

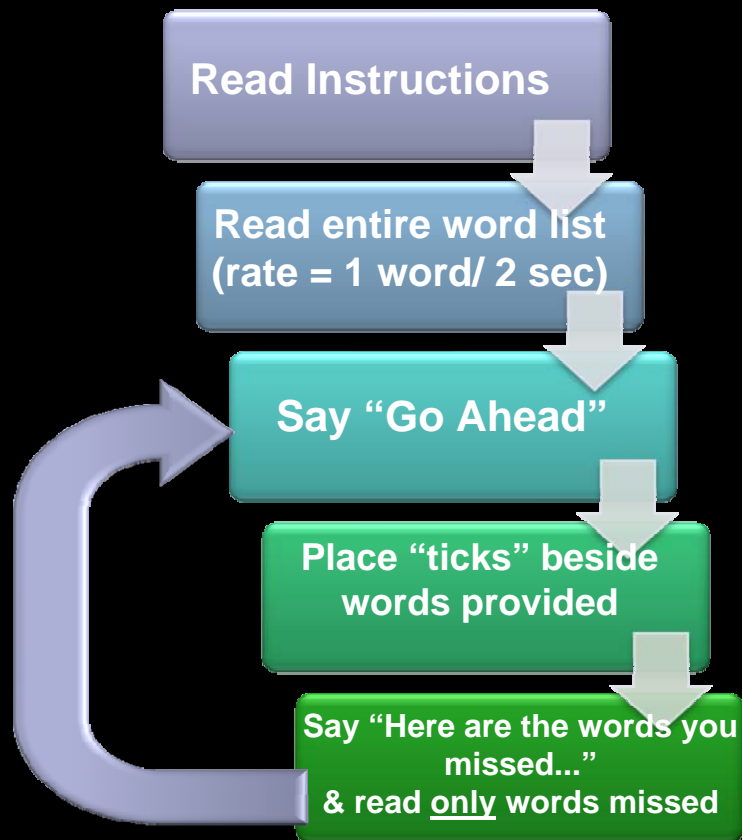
Test 1: Selective Reminding Test

Background

- **Assesses verbal learning and retrieval**
 - Examiner reads list of 12 words
 - Subject instructed to recall list
 - Examiner re-reads only missed words
 - Patient instructed to recall entire list
 - Continue for 6 trials

Test 1: Selective Reminding Test

Administration & Recording



MEASURE Study STUDY DAY 1 (SD1) - VISIT 1

Subject ID#

Site # Subject # Date of Visit: D D M M M Y Y Y Y

SELECTIVE REMINDING TEST - FORM 1

For each trial, please place a ✓ in the appropriate column when the word is recalled.

	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5	Trial 6
1. direction	✓	✓				
2. memory		✓				
3. owner	✓					
4. mountain						
5. victim	✓	✓				
6. city		✓				
7. victory		✓				
8. dream	✓					
9. hotel						
10. wife		✓				
11. virtue	✓					
12. slave	✓	✓				

Test 2: Symbol Digit Modality Test

Administration & Recording



SYMBOL DIGIT MODALITIES TEST - FORM 3

+	()	>	⊥	÷	÷	⊥	Γ
1	2	3	4	5	6	7	8	9

For each symbol, please ✓ for a correct response and ✗ for an incorrect/wrong response.

(⊥	÷	(⊥	>	÷	Γ	(>	÷	(>	(÷
3	5	7	2	8	4	7	9	2	4	7	2	4	2	7
✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✗	✓	✓

Γ	>	(÷	⊥	>	⊥	Γ	(÷	>	÷	Γ	⊥	(
9	4	2	7	5	4	8	9	2	7	4	6	9	8	2
✓	✓	✗	✓											

Test 3: Paced Auditory Serial Addition Test Background

- Test of sustained attention, concentration and information processing speed
- Requires patients to monitor a series of 61 audiotaped digits while adding each consecutive digit to the one immediately preceding it

Audio:	5	(+)	4	(+)	8	(+)	1	(+)	3
			↓		↓		↓		↓	
Response:			9		12		9		4

- **Materials:**
 - Cassette Tape
 - Sample Items Page
 - Recording Form
- **Notes:**
 - Important that this is done in a quiet room with no distractions
 - Severe auditory or speech problems may invalidate results

Limitations when interpreting cognitive test results

- Confounders include:
 - Depression
 - Fatigue
 - Pain
 - Medication
 - Cannabis?

Cognitive correlates

brain imaging

MRI: lesion change over time

- MRI with Gd every two weeks
- 6 months of scanning
- > 90 new lesions
- Little change in physical disability
- 5 secs = 1 week in the patient's life



Acknowledgement: the late Prof. W. I. McDonald et al: Institute of Neurology, Queen Square

Cognitive correlates

brain imaging: atrophy

- Atrophy has emerged as the most robust correlate of cognitive dysfunction

Cognitive correlates

brain imaging: fMRI

- Growing literature comparing patterns of activation to those seen in healthy subjects
 - PASAT
 - Working memory
- Similar results: even if MS patients did not do more poorly than healthy controls they required additional cerebral activation to achieve this.
- Imaging reveals the attempts at compensation
- Brain plasticity

Cognitive dysfunction:

Approaches to Rehabilitation

- Compensatory strategies ++
 - Maximize residual cognitive strengths
 - Practice, routine, structure

Cognitive dysfunction:

Approaches to Rehabilitation

- Remedial strategies -
 - Improve cognitive abilities
 - Remedial
 - eg: Computer based techniques for enhancing attention and speed of processing, improving memory

Cognitive dysfunction:

Approaches to Rehabilitation: medication

- Psychostimulants: Amantadine, methylphenidate
 - On balance, weak benefits
- Steroids
 - Pulsed steroids
 - No long term cognitive harm
 - May restore, in part, cognition after catastrophic attack
- Cyclophosphamide
 - Possible benefits in CP MS, but study hurt by the absence of a control group.

Cognitive dysfunction:

Approaches to Rehabilitation: medication

- Cholinergic drugs
 - Donepezil hydrochloride
 - Rivastigmine (Parry et al, 2003)

Cognitive dysfunction:

Approaches to Rehabilitation: Disease modifying drugs

- ✓ Interferon beta-1a (Avonex)
- ✗ Glatiramer acetate
- ✓ Interferon beta-1a (Rebif)
- ✓ Interferon beta-1b (Betaseron)

Cognitive dysfunction:

Breaking the news

Multiple Sclerosis and Depression: Insights from brain imaging



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Research

MS patients needed for a series of
cognitive studies.