

Cognitive Changes in Demyelinating Diseases

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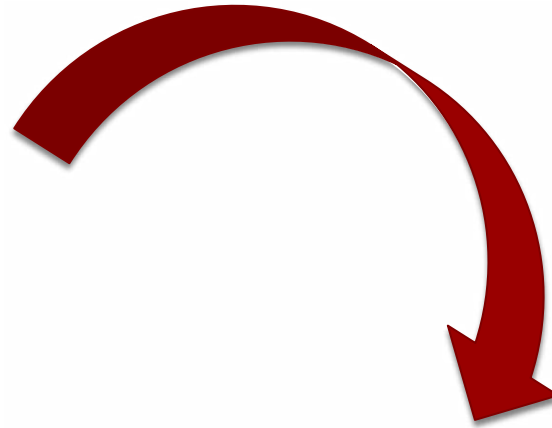
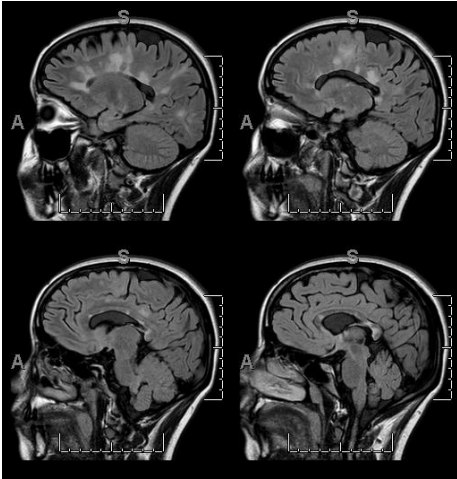
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Role of Neuropsychology

Neuropsychology

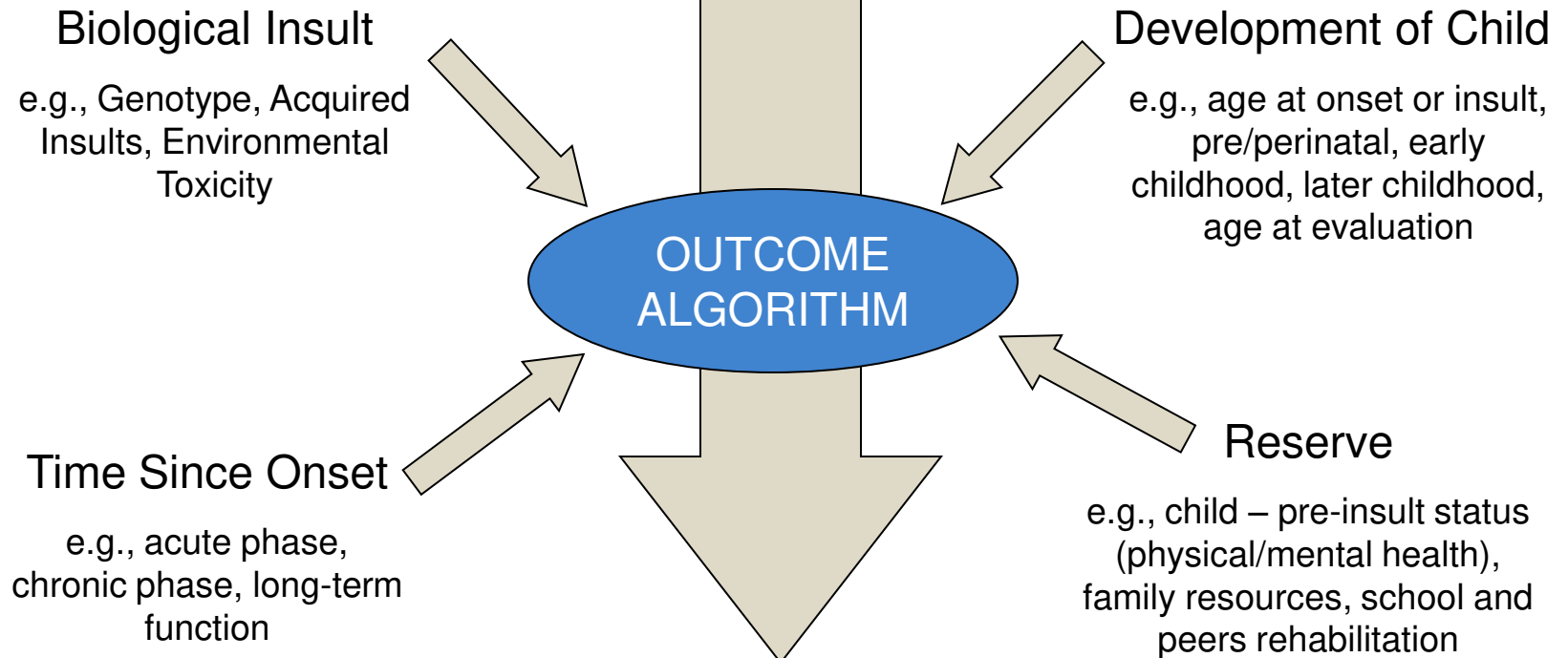
- Application of principles of assessment and intervention based on the scientific study of human behavior as it relates to normal and abnormal functioning of the central nervous system (CNS)
- Dedicated to enhancing the understanding of brain-behavior relationships and the application of such knowledge to human problems

Functional Impairment



Dennis, 2000

MEDICAL CONDITION



COGNITIVE PHENOTYPE

Areas that Influence Performance

- Effort
- Fatigue
- Cooperation
- Motivation
- Sleep
- Emotional functioning (Depression, Anxiety)
- Behavioral Regulation
- Medication
- Sensory impairment

Our Research Journey

Role of Neuropsychology

- Clinic Role
 - Screening Battery
 - Performance-based measures
 - Parent ratings – behavioral, emotional, school functioning
- Demyelinating Diseases
 - Brain-based: MS, ADEM, CIS, NMO* (relative sparing)
 - Non-Brain-based: TM

Domains Assessed	Measures
Processing speed	WISC-IV/WAIS-III Symbol Search Symbol-Digit Modalities Test (SDMT)
Fine-motor speed and dexterity	Grooved Pegboard
Visual-motor integration	Beery-Buktenica Developmental Test of Visual-Motor Integration (VMI)
Visual perception	VMI Visual Perception (VP)
Simple auditory attention Speeded visual attention and sequencing	WISC-IV/WAIS-III Digits Forward Trail Making Test, Part A
Working memory	WISC-IV/WAIS-III Digits Backward
Verbal learning and memory	California Verbal Learning Test – Children’s Version (CVLT-C)/Second Edition (CVLT-II)
Speeded complex attention and sequencing	Trail Making Test, Part B
Verbal Fluency	D-KEFS Letter Fluency

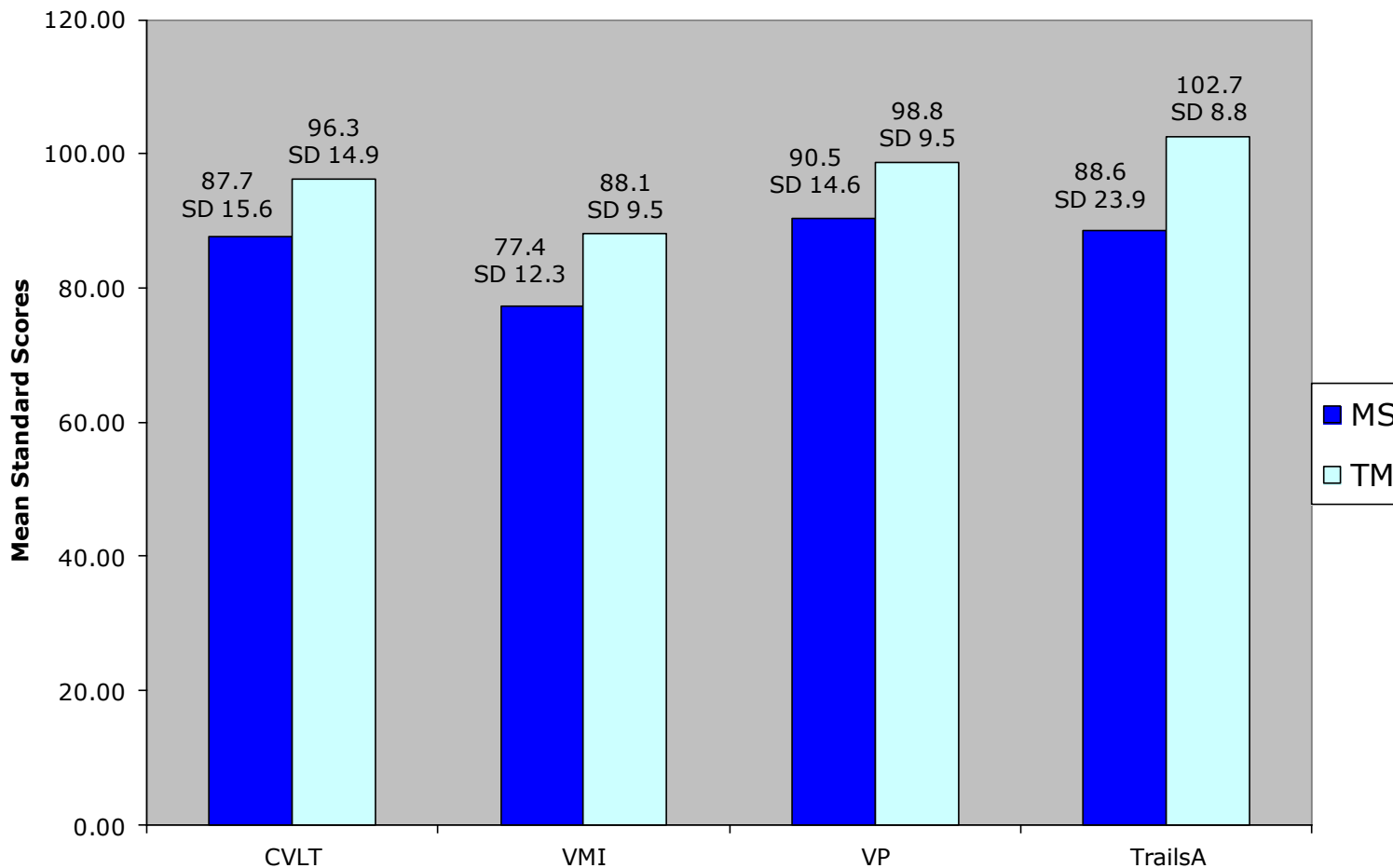
Cognitive Functioning and School Performance in Pediatric Demyelinating Diseases: A comparison between MS and TM

- Study Aims
 - To compare neuropsychological performance between TM and MS to investigate cognitive problems associated with pediatric MS
 - To explore caregiver ratings of school performance
- Hypotheses
 - Children diagnosed with MS will perform more poorly on tests of neuropsychological functioning as compared to children diagnosed with TM
 - Caregivers of MS patients will report a higher rate of school problems compared to parents of TM patients

Cognitive Functioning and School Performance in Pediatric Demyelinating Diseases: A comparison between MS and TM

- 18 MS and 22 TM subjects, aged 5 to 18 years
- Completed screening battery
- MS group showed greater difficulty in verbal memory, attention, visual-motor integration, and visual perception

MS vs. TM: Statistically Significant Findings



Cognitive Functioning and School Performance in Pediatric Demyelinating Diseases: A comparison between MS and TM

- No significant differences were found between MS and TM groups on school performance
 - Approximately 35% of participants in each group are below average or failing in at least one subject

	Failing	Below Average	Average	Above Average
Reading/ English/ Language Arts				
History/ Social Studies				
Arithmetic/ Math				
Science				

Neuropsychological Outcomes in Pediatric Transverse Myelitis: What do we know?

- Literature
 - Two papers on clinical presentation of pediatric idiopathic TM patients
 - Pidcock et al, 2007
 - Describes cohort of 47 pediatric TM patients clinical characteristics and functional outcomes
 - No mention of cognitive or psychological problems and/or outcomes
 - Trecker et al, 2009
 - Survey of parents of 20 patients diagnosed with indicated 90% desired consultation with psychiatry as part of their child's care
 - Qualitative reports of cognitive and psychological problems but no data to support this
- Clinic Observations
 - 41.7% TM patients received referral for mental health services (individual therapy)
 - 29.2% TM patients were referred for a full neuropsychological evaluation

Cognitive functioning in pediatric transverse myelitis

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Multiple Sclerosis Journal
0(0) 1–6
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sagepub.co.uk/journalsPermissions.nav
DOI: 10.1177/1352458512466606
msj.sagepub.com



- 24 TM subjects
 - Age range 5 to 18 years
 - mean = 11 years
 - 63% female

Table 1. Medical and demographic information.

Variable	Mean	SD	Range
Age (years) at onset	9.67	4.84	1–17
Age (years) at evaluation	11.46	3.36	5–18
Time since symptom onset (months)	22.13	39.37	1–135
Hauser Ambulation Index	2.58	2.90	0–9
Variable	n	%	
On medication ^a	11	45.80	
Cervical	13	54.20	
Longitudinally extensive lesion ^b	13	54.20	
Female	15	62.50	
Right handed	21	87.5	
Race/ethnicity			
White	15	62.50	
Black or African-American	1	4.20	
Hispanic or Latino	6	25.00	
American Indian or Alaska Native	1	4.20	
Asian	1	4.20	

^aIncluded medication known to have potential cognitive impairment (i.e. selective serotonin reuptake inhibitors (SSRIs), GABAergic medications, tricyclic antidepressants, and anticholinergic agents);

^bdefined as lesion spanning greater than or equal to three cord segments.

Rate of Impairment: TM

Domain	TM
Fine-motor coordination	43%
Memory	
Initial Learning	33%
Following Practice	13%
Attention	41%
Fluency	25%
Parent-Reported Attention Problems	30%
Parent-Reported Depression	30%
School Problems	33%
Referral for Additional Testing	29%

Clinical & Psychosocial Characteristics

Table 3. Clinical and psychosocial characteristics.

Variable	<i>n</i>	%	Mean	SD	Range
School problems	8	33.30	—	—	—
Referral for further testing	7	29.20	—	—	—
Depression			53.78	11.42	37–82
At-risk	5	21.70	—	—	—
Clinically significant	2	8.70	—	—	—
Attention problems			50.13	10.04	36–65
At-risk	7	30.40	—	—	—
Clinically significant	0	0	—	—	—
Sleep/rest fatigue Parent			66.86	15.19	42–92
Mild	9	42.90	—	—	—
Severe	6	28.60	—	—	—
Self			66.76	17.29	38–100
Mild	8	38.10	—	—	—
Severe	0	0	—	—	—
General fatigue Parent			57.81	20.47	4–88
Mild	7	33.30	—	—	—
Severe	11	52.40	—	—	—
Self			62.29	19.60	21–96
Mild	3	14.30	—	—	—
Severe	9	42.90	—	—	—

Depression and attention problems are based on Behavior Assessment System for Children, Second Edition (BASC-2) Parent report; fatigue scores are derived from the Pediatric Quality of Life (PedsQL) Multidimensional Fatigue Scale.

Conclusion

- Higher than expected rate of cognitive deficits
- Deficits did not correlate with depression or medication use but qualitative analysis of data suggests that fatigue may play an important role
- Highlights need for multi-disciplinary treatment approach to address cognitive and psychological needs
- *Could there be BRAIN BASED PATHOLOGY IN TRANSVERSE MYELITIS?*

Neuropsychological Outcomes in NMO: What do we know?

- Similar performance in MS and NMO groups suggesting possible brain involvement in NMO (Blanc et al., 2008)
- Patients with NMO showed problems with learning and memory, processing speed, and attention during acute relapse compared to controls (He et al., 2011)
 - Findings correlated with imaging on DTI showing abnormalities in various areas in the brain
- 54% of NMO patients had cognitive impairment in areas of memory, executive function, attention, processing speed (Blanc et al., 2012)
 - Findings correlated with imaging findings including decreased brain volume

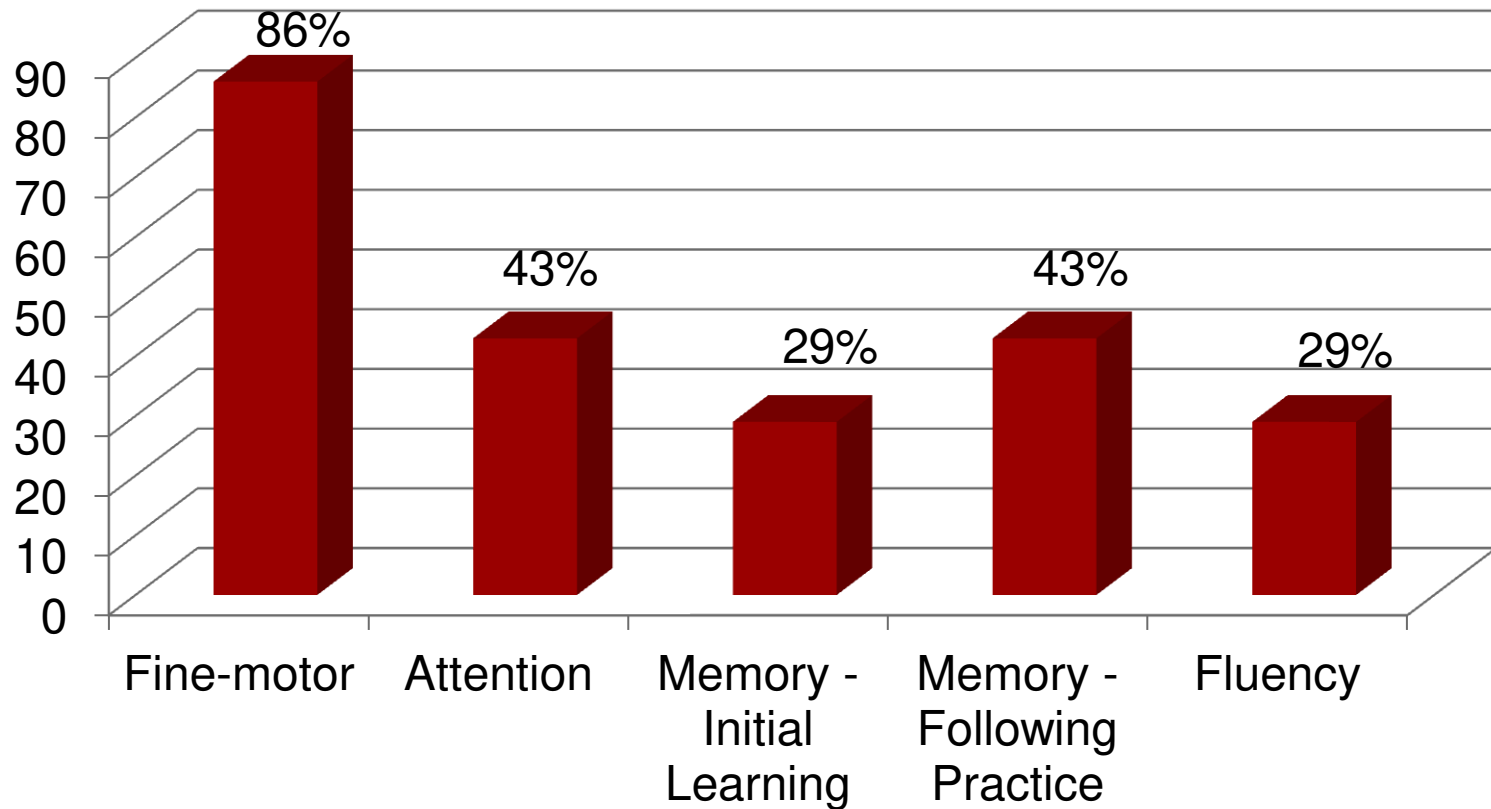
Cognitive Functioning in NMO

Table 1. *Demographic Variables*

	Mean	SD	Range
Age (years) at onset	10.71	3.35	6-16
Age (years) at testing	12.42	3.69	9-19
Disease Duration (years)	1.71	1.25	0-3
	<i>n</i>	%	
Female	7	100	
Right-handed	6	86	
Ethnicity			
Hispanic or Latino	3	43	
Black or African-American	4	57	

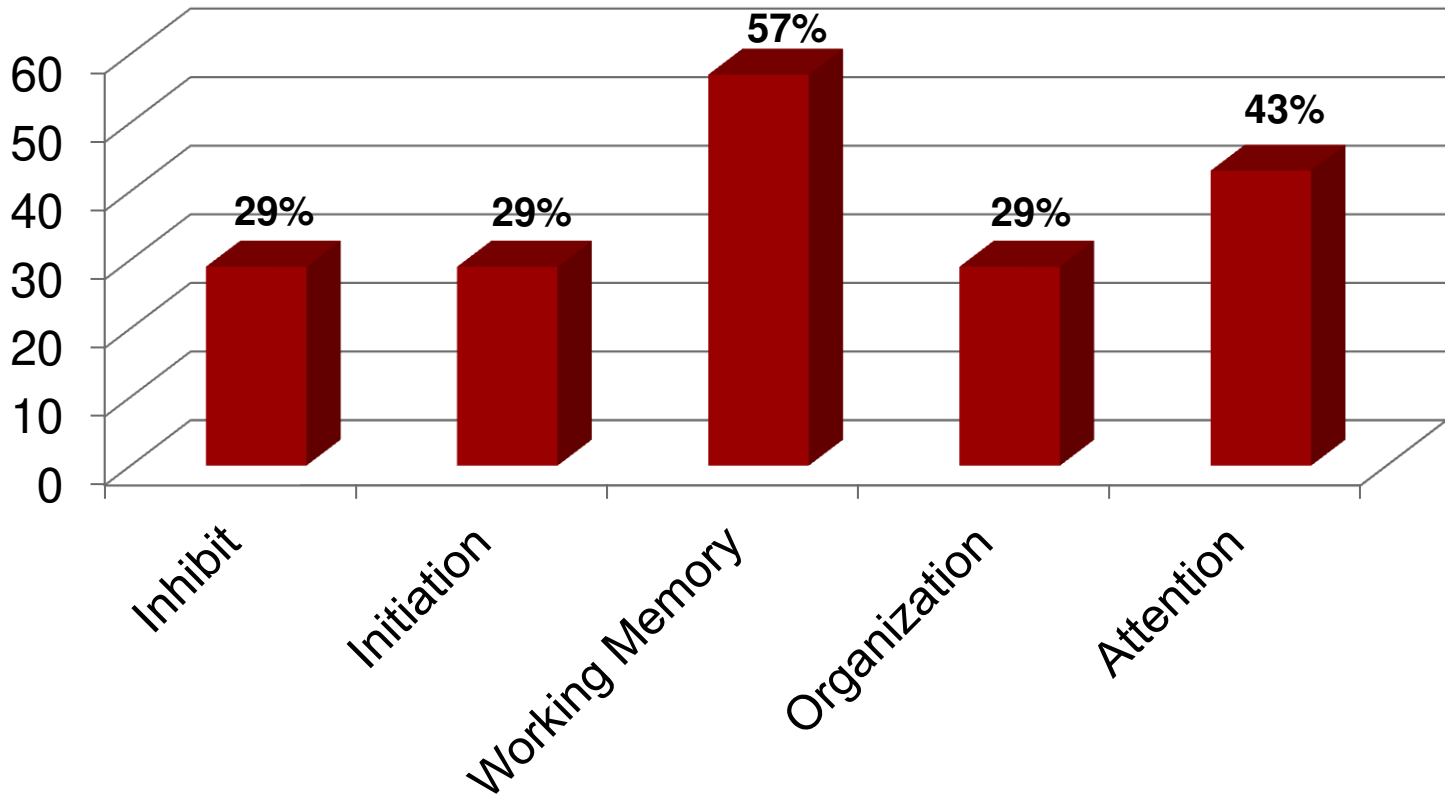
Performance-based Tests

Impairment Rates in NMO



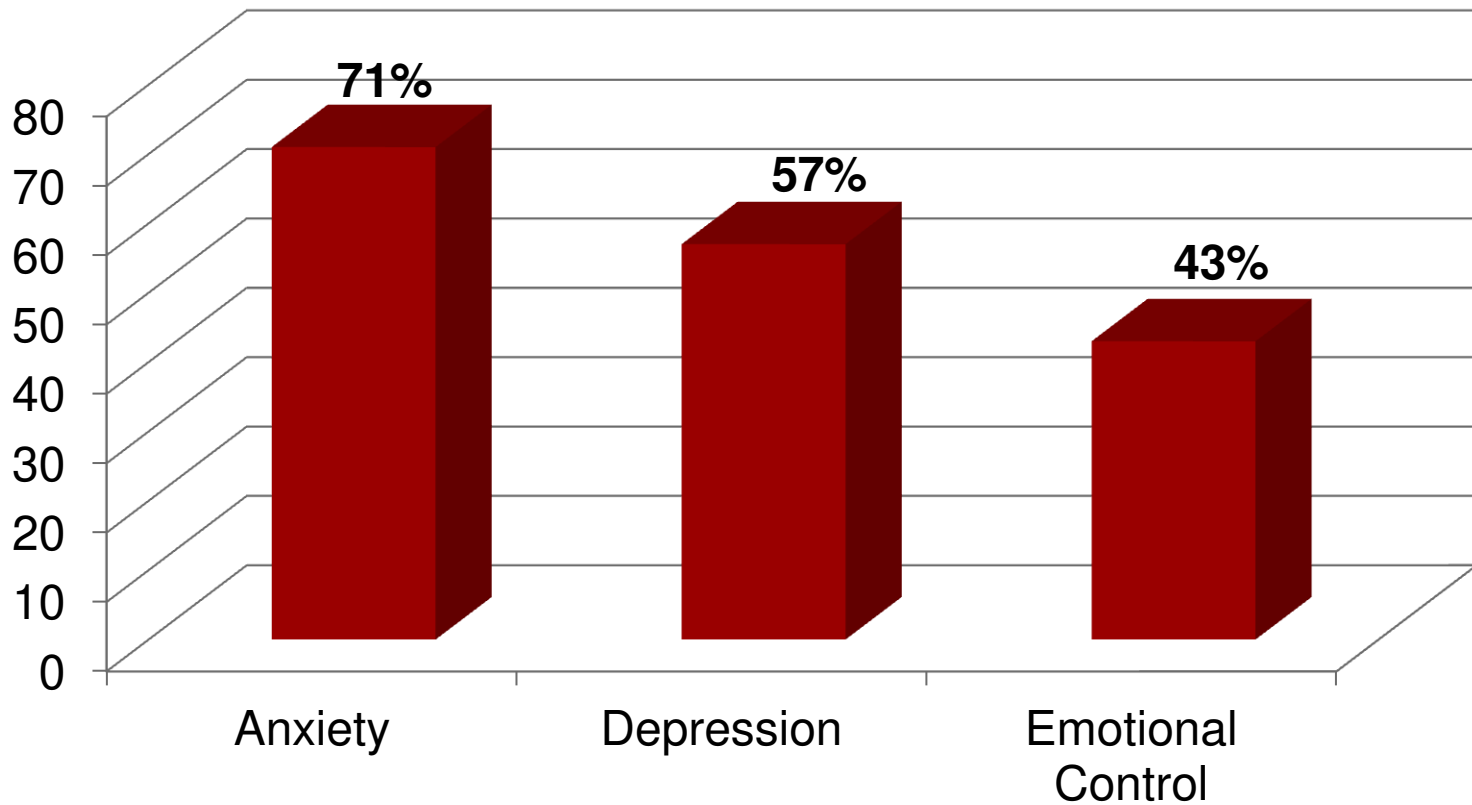
Parent-Reported Rates of Impairment

Attention & Executive Function in NMO



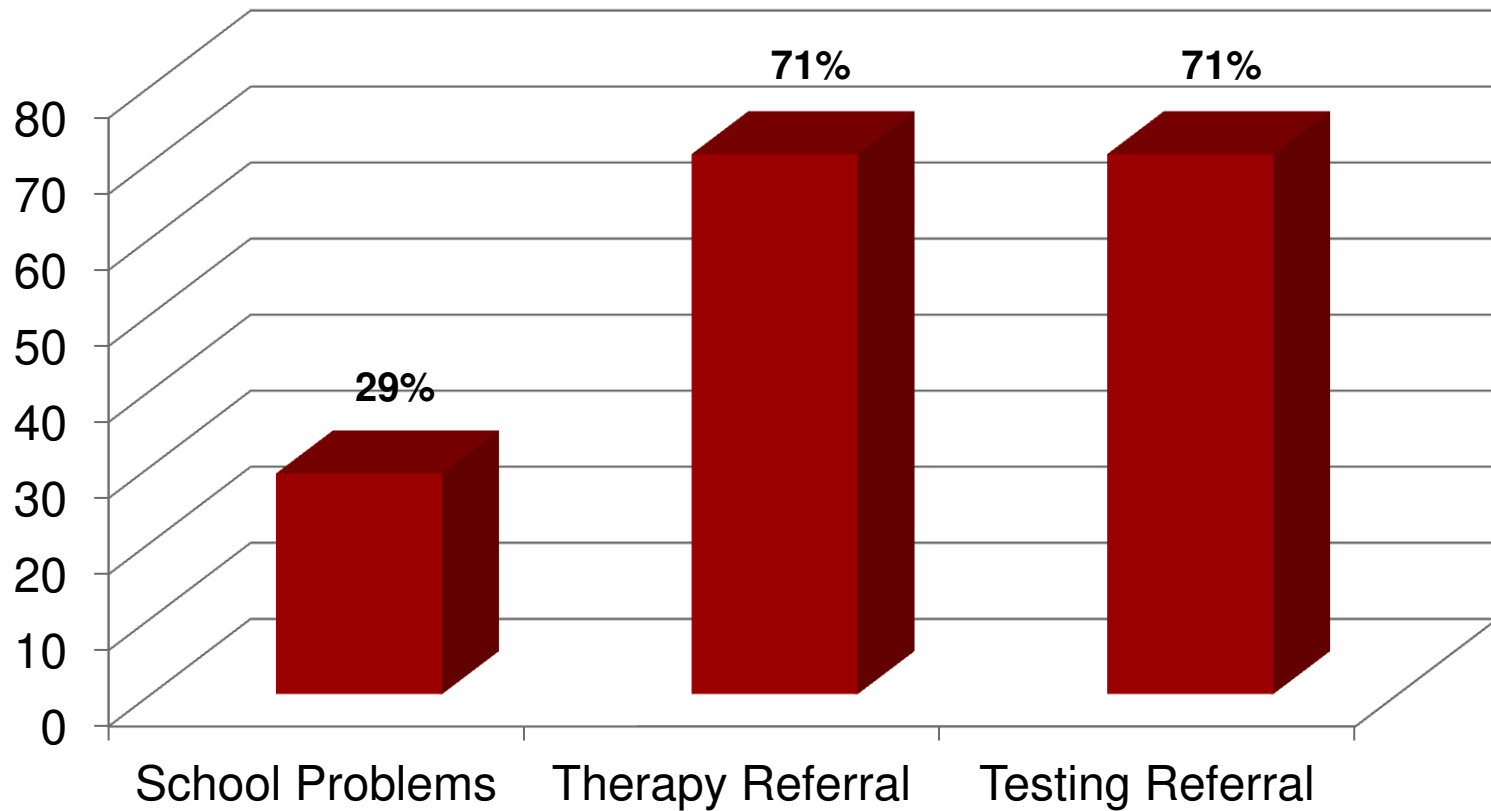
Parent-Reported Rates of Impairment

Emotional Functioning in NMO

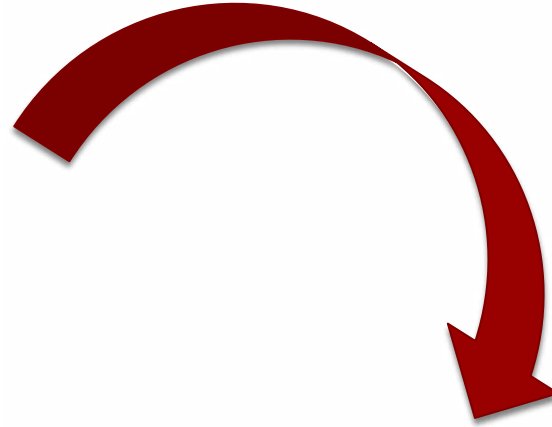
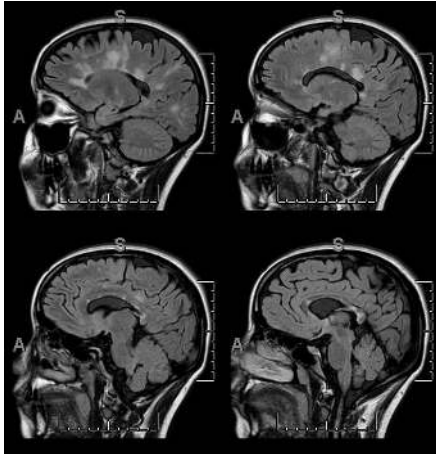


Other Clinical Variables

School Problems and Referrals in NMO



Challenging our understanding



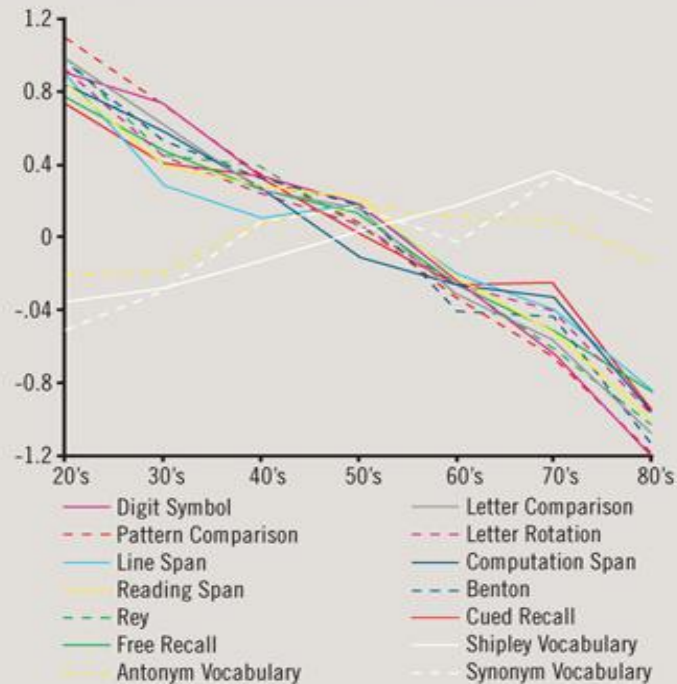
Who is a Candidate for Assessment?

- You and those who know you best are in the best position to evaluate changes in cognition over time
- Functional impact – cognitive problems interfere with daily functioning
- If you have concerns, speak with your physician regarding a referral for this evaluation
- Keep in mind cognitive changes that come with normal aging!

Cognitive Decline & Normal Aging

SLIDE 1

Normal Aging and Cognitive Test Performance¹



There is linear decline by age on measures of attention, concentration, rapid visuospatial analysis, and episodic memory.

Resistant to age are aspects of semantic knowledge (vocabulary) and abstraction.

Reprinted with permission: Park DC, et al. Models of visuospatial and verbal memory across the adult life span. *Psychology and Aging*. American Psychological Association. Copyright 2002.

Intervention

- Multi-disciplinary approach
- Medical
 - Medication to address cognitive and emotional functioning, fatigue
- Cognitive
 - Cognitive rehabilitation
 - “Cognitive coaching”
 - Ex: Cueing strategies to address memory problems
- Educational
 - Special Education services
 - Classroom accommodations
- Psychological
 - Therapy
 - Ex: Cognitive-Behavioral Therapy to address depression

Conclusion

- Patients with demyelinating diseases have complex and often changing needs
- Require support for a team of specialists
- Importance of regular surveillance by multi-disciplinary team to inform appropriate intervention

Acknowledgements: Our Team

- Benjamin Greenberg, MD, MHS
- Donna Graves, MD
- Audrey Ayres, RN BSN
- Darrell Conger
- Allen Desena, MD
- Alice Ann Holland, PhD
- Samuel Hughes
- Linda McCowen
- Caroline Mooi, LMSW
- Katherine Treadaway, LCSW

