Longitudinal evaluation of cognition in multiple sclerosis: impact of cognitive reserve

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Introduction

- Cognitive impairment in MS can be evident in multiple domains, including: complex attention, information processing speed, learning and memory, and executive function.[1-2] Cognitive outcomes in people with MS (PWMS), however, are highly variable; for instance, some PWMS remain cognitively intact despite advanced disease.[3]
- Cognitive reserve (CR) theory postulates that individuals with higher levels of intellectual enrichment can tolerate more pathology than others before exhibiting cognitive impairment and functional decline. In the context of MS, CR may buffer patients against potential long term cognitive effects of the disease.[4]
- The present study used neuropsychological data from a sample of individuals with early-phase relapse remitting multiple sclerosis (RRMS) at both baseline and 3-year follow up. The goal was to determine if individuals with varying levels of CR demonstrated different cognitive outcomes at follow-up, even very early in their disease course.
- **Hypotheses:**

1. PWMS will perform worse on cognitive measures than healthy controls (HC).
2. The relationship between baseline and follow-up cognitive scores will be mediated by CR.

Methods

Participants

- 32 individuals with RRMS were recruited from the MS Clinic of the Ottawa Hospital. In addition, 32 age-, education- and IQ-matched healthy controls were recruited from the community (see Table 1).
- Participants in the MS group had a mild level of physical disability (EDSS = 1.83(1.18)) and disease duration less than 10 years (4.35 yrs (3.09)).

Table 1: Demographics

	MS	HC	*p*
Age	40.09 (9.21)	42.22 (11.63)	0.42
Education	14.86 (1.92)	15.42 (2.90)	0.26
IQ	110.18 (6.83)	113.05 (7.19)	0.11

Procedure

- Participants completed an extensive battery of neuropsychological tests (as indicated below) at both baseline and three year follow-up.

Analyses

- Statistical significance was set at $p < 0.05$ (two-tailed). Mixed analyses of variance (ANOVA) were performed to assess group differences over time. Regression analyses evaluated whether CR mediated the relationship between baseline and follow-up cognitive performance.

Measures

- Cognitive reserve was assessed using individuals' level of education (in years) and their score on the North American Adult Reading Test (NAART), a task which measures a person's ability to pronounce phonetically irregular words that is commonly used to estimate premorbid IQ.
- The cognitive domains investigated, and the tests used to assess cognitive performance were as follows:

Information Processing Speed	▪ Symbol Digit Modalities Test – SDMT (oral) ▪ Paced Auditory Serial Addition Test - PASAT (3 sec)
Language	▪ Controlled Oral Word Association Test - COWAT (FAS & Animals)
Learning	▪ Word List Learning – Learning and Memory Battery - LAMB (Total Recall) ▪ Brief Visuospatial Memory Test – BVMT Revised (Immediate Recall Total)
Memory	▪ Word List Learning – Learning and Memory Battery - LAMB (Delayed Recall) ▪ Brief Visuospatial Memory Test - BVMT Revised (Delayed Recall)
Executive	▪ D-KEFS Sorting Test (Confirmed Correct Sort) ▪ D-KEFS Tower Test (Total Achievement Score)

Results

Hypothesis 1

- PWMS performed worse than HC on tests of information processing speed at both baseline and at follow-up ($F(1,59) = 4.67$, $p = 0.04$) (see Table 2). On memory, PWMS performed worse than HC at baseline on LAMB – delayed recall; on BVMT- delayed recall, PWMS performed worse than HC at both baseline and follow-up ($F(1,62) = 4.95$, $p = 0.03$) (see Table 3).
- There was a group x time interaction for executive functioning ($F(1,62) = 8.68$, $p < 0.1$), such that HC improved over time while PWMS showed no significant change over time (see Table 4).
- There were no group differences observed in language or learning.

Hypothesis 2

- Although baseline cognitive performance predicted follow-up performance, this relationship was not mediated by the CR variables.
- Thus, the CR variables did not have an influence on how cognition in PWMS changed over time in this sample.

Table 2: Group differences in information processing speed at baseline and follow-up

	SDMT		PASAT	
	Baseline	**Follow-up**	**Baseline**	**Follow-up**
HC	64.17(8.71)	67.87(1.35)	53.27(8.11)	54.60(6.99)
MS	61.90(10.39)	63.45(1.77)	48.26(10.84)	50.64(7.99)

Table 3: Group differences in memory at baseline and follow-up

	LAMB – delayed recall		BVMT – delayed recall	
	Baseline	**Follow-up**	**Baseline**	**Follow-up**
HC	14.37(0.98)	10.72(1.35)	14.09(1.35)	10.09(1.78)
MS	13.97(1.43)	9.66(1.77)	14.23(1.41)	9.16(2.01)

Table 4: Group differences in executive functions at baseline and follow-up

	D-KEFS - Sorting Test		D-KEFS - Tower Test	
	Baseline	**Follow-up**	**Baseline**	**Follow-up**
HC	10.31(1.82)	11.03(1.82)	17.90(3.71)	20.81(3.54)
MS	10.78(1.64)	10.50(1.76)	18.12(3.00)	19.09(2.63)

Conclusion

- Hypothesis 1 was supported in that PWMS performed worse than HC in some cognitive domains (information processing speed, memory and executive functioning), consistent with the literature.
- Nonetheless, no group differences were observed in language and learning. The latter, in particular, is unexpected given that learning measures are typically more sensitive to cognitive impairment than memory per se in PWMS.[5]
- Hypothesis 2 was not supported given that the CR variables did not appear to influence cognitive outcome at follow-up.
- The reason these findings are not consistent with others in the literature is likely the result of the unique characteristics of this sample.
- First, the sample was restricted to early-phase RRMS with a disease duration less than 10 years. As such, these individuals are typically less disabled and more homogenous compared to those in other studies.[6-8] This may account for why their cognition did not decline to a significant degree over the study interval.
- Second, the degree of CR in this sample was less variable than that observed in other studies.[6-8] All individuals had what other studies would refer to as average to high reserve given that they all had at least a high school education. Attempts were made to control for this by using CR as a continuous variable, rather than a dichotomous one. Despite these efforts, the sample lacked sufficient variability to demonstrate an impact of CR.
- The fact that this sample had average to high reserve may well have been a protective factor which accounted for the relative stability of cognition over time.

Selected references

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