A simple measure of Cognitive Reserve predicts cognitive performances of MS patients more consistently than clinic-demographic and MRI parameters

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BACKGROUND

Cognitive impairment (CI) is estimated to affect 40% to 70% of patients with multiple sclerosis (MS). Individual cognitive reserve (CR) can mitigate the detrimental effect of the disease on cognitive function.

OBJECTIVES

To assess, in a large group of MS patients, the relationship between two CR measures and cognitive performances after controlling for multiple clinical, demographic and magnetic resonance imaging (MRI) parameters.

METHODS

- **Study population:** 115 patients diagnosed with clinically isolated syndrome (CIS, N = 4), relapsing-remitting MS (RRMS; N = 98) and secondary-progressive MS (SPMS; N = 13) (demographic characteristics are summarized in Tab. 1).
- **Data acquired (on the same day):**

• Neurological evaluation including the Expanded Disability Status Scale (EDSS)
• Fatigue Severity Scale (FSS) and Chicago Multiscale Depression Inventory (CMDI)
• Two measures of CR:
- number of years of formal/academic education (EDU)
- vocabulary knowledge (VOC), as assessed by the vocabulary task of the Wechsler Abbreviated Scale of Intelligence
• Neuropsychological (NP) evaluation → Rao's Brief Repeatable Battery (BRB) + Stroop Test →10 NP tests (failed test = ≤2SD vs normative value)
• 3T-MRI study, including T2, T2-FLAIR and a high-resolution 3D-T1 sequences

- **Data analysis:**

A linear multivariate regression analysis – including CR measures as well as clinic-demographic parameters (age, gender, disease duration, EDSS, FSS, CMDI) and MRI metrics (T2-lesion volume [T2LV], normalized brain volume [NBV], normalized grey matter volume [NGMV], normalized white matter volume [NWMV]), as covariates - was used to investigate the best independent predictors of each NP test score (Tab. 2).

Tab. 1

	Mean ± SD
Age, y	38.28 ± 10.9
Sex (M/F)	38/77
Edu, y	12.6 ± 3.7
Dis. Duration, m	136.98 ± 116.5
EDSS	2.82 ± 2
VOCAB-WAIS	41.54 ± 16.2
SRT-LTS	38.47 ± 15.2
SRT-CLTR	26.66 ± 15.3
SPART	17.45 ± 5.5
SDMT	34.05 ± 13.1
PASAT 3"	34.97 ± 14.1
PASAT 2"	27.38 ± 10.4
SRT-D	7.32 ± 2.6
SPART-D	5.77 ± 2.3
WLG	19.18 ± 4.9
STROOP	86.36 ± 56
CMDI	73.46 ± 21.6
FSS	33.29 ± 15.8

Tab. 2

Outcome	Predictor	β	p
SRT-LTS p < 0.0001 (R^2= 0.257)	**VOC**	**0.316**	**0.001**
SRT-CLTR p < 0.0001 (R^2= 0.288)	VOC	0.363	≥0.0001
SPART p < 0.0001 (R^2= 0.292)	**VOC**	**0.330**	**0.001**
SDMT p < 0.0001 (R^2= 0.500)	VOC	0.471	> 0.0001
	T2-VOI	-0.246	0.003
PASAT3" p < 0.0001 (R^2= 0.292)	**VOC**	**0.428**	**> 0.0001**
PASAT2" p = 0.003 (R^2= 0.213)	VOC	0.332	0.001
SRT-D p = 0.001 (R^2= 0.210)	**VOC**	**0.293**	**0.002**
SPART-D p > 0.0001 (R^2= 0.346)	VOC	0.412	> 0.0001
	T2-VOI	-0.263	0.006
WLG p = 0.001 (R^2= 0.225)	**VOC**	**0.325**	**0.001**
STROOP p > 0.0001 (R^2= 0.253)	VOC	-0.305	0.001
	EDSS	0.325	0.001

DISCUSSION AND CONCLUSIONS

- A simple measure of CR, such as the VOC, was the stronger and more consistent predictor of cognitive performances as measured by Rao's BRB and Stroop Test in a large single-center group of MS patients.
- EDSS score also emerged as an independent predictor of cognitive performance at executive functions subtest (Stroop Test).
- T2-VOI also emerged as an independent predictor of cognitive performance at sustained attention (SDMT) and visuo-spatial memory delayed recall (SPART-D) subtests.
- VOC might be used by clinicians as a measure of CR to identify patients at greater risk of future CDs and target them for early cognitive rehabilitation intervention.

RESULTS

A higher VOC was the best independent predictor (0.01<p<0.001) of better performance at all BRB subtests and Stroop Test. T2-VOI and EDSS also emerged as independent predictors of cognitive performances, but only in a few BRB subtests.

FUTURE RESEARCH

- Future multi-center studies with a longitudinal design will have to further assess the utility of this simple CR measure as a clinical-meaningful predictor of cognitive performances in MS patients.
- It would also be very interesting to extent the investigation of the CR in the pediatric MS population.

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