Cognitive reserve is associated with better cognitive outcome and socio-professional attainment in both adult and pediatric-onset multiple sclerosis

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BACKGROUND

•Cognitive impairment (CI) is increasingly appreciated in pediatric-onset multiple sclerosis (POMS).
•The concept of cognitive reserve (CR) has been proposed to bridge the gap between the degree of brain damage and its clinical manifestations.
•While the role of CR in adult-onset multiple sclerosis (AOMS) patients is being recognised, information in the pediatric-onset MS (POMS) population is limited.

OBJECTIVE

This study aims at comparing cognitive outcome and socio-professional attainment in POMS versus AOMS patients and the relevant demographic and clinical correlates, including CR.

METHODS

Inclusion criteria
•Confirmed diagnosis of MS (Polman, 2011) before the age of 18 years (POMS patients)
•Diagnosis of MS with onset of the disease after 18 years (AOMS patients)
•Informed consent

Cognitive assessment
•The ***neuropsychological test battery*** included:
-Verbal learning and delayed recall through the Selective Reminding Test [SRT]; and Selective Reminding Test Delayed [SRTD] (Rao SM, 1990).
-Visuospatial learning and delayed recall through the Spatial Recall Test [SPART] and Spatial Recall Test–Delayed [SPARTD] (Rao SM, 1990) .
-Sustained attention and concentration through the Symbol Digit Modalities Test [SDMT]
-Expressive language through a Semantic Verbal Fluency Test (Spinnler H, 1987)
-Stroop test
•***Fatigue*** *was* be assessed through the the Fatigue Severity Scale (FSS). (Krupp LB 1989).
•***Depression*** through the Montgomery and Asberg Depression Rating Scale (Montgomery SA, 1979).
The neuropsychological test battery was administered in a single session. The whole assessment required on average 45 minutes.

Cognitive impairment (CI)
•CI was defined as the failure of at least 3 tests on the basis of the Italian normative data.

***Cognitive Reserve* (CR)**
•CR was estimated using years of education and premorbid Intelligent Quotient through the Italian version of the National Adult reading Test (Colombo L, 2002) , the "Test d'Intelligenza Breve" (TIB) (Sartori G. 1997) and parental socio-economic status (SES) evaluated on the Barratt Simplified Measure of social status (BSMSS) (Barratt W, 2006).

Psychosocial assessment
•We used the Work and Social Adjustment Scale (WSAS) (Chambon, 1992). This a 13-item scale providing an estimation of good "social functioning" with a satisfying employment valuation. Unemployment rate has been also evaluated.

Statistical analysis
Group comparisons were performed using the Student t test, Mann-Whitney test and chi^2 test when appropriate, with Bonferroni's correction for multiple comparisons.
Cognitive evaluation
Cognitive performance on the BRB was assessed through the Italian normative values (Amato MP, 2006). Prognostic factors for social insertion were assessed using a logistic multivariable regression analysis including WSAS classification as dependent variable. Onset classification (pediatric vs adult) was included as covariate together with age, sex, CR (premorbid IQ and education), EDSS, cognitive impairment, BSMSS score, treatment with disease modifying drugs, relapses in the year preceding the inclusion, fatigue and depression scores,
Prognostic factors for CI were assessed using a logistic multivariable regression analysis including CI as dependent variable. Onset classification (pediatric vs adult) was included as covariate together with age, sex, CR (premorbid IQ and education), EDSS, BSMSS score, treatment with disease modifying drugs, relapses in the year preceding the inclusion, fatigue and depression scores.
All statistical analyses were performed using SPSS software, version 23.0, running on Windows (SPSS, Chicago, IL, USA, 2002).

RESULTS

Table 1. Demographic and clinical characteristics of study sample

	Total sample (226)	POMS (111)	AOMS (115)	P
Age, mean (SD) years	35,1 (11,1)	32,0 (9,7)	38,8 (9.3)	*<0,001*
Sex, F/M	157/69	74/37	68/47	Ns
Education, mean (SD) years	13,0 (2,8)	13,0 (3,1)	13,3 (4,8)	Ns
Disease duration, mean (SD) years	14,4 (9,2)	16,9 (9,8)	12,1 (7,9)	*<0,001*
Age at onset, mean (SD) years	18,9 (11,8)	15,5 (2,3)	27,3 (8,0)	<0,001
EDSS, mean (SD)	2,4 (1,6)	2,4 (1,6)	2,4 (1,8)	Ns
DMTs (#/%)	208	104 (93%)	104 (88,7)	Ns

Legend: POMS: pediatric onset multiple sclerosis; AOMS: adult onset multiple sclerosis; SD, standard deviation; F/M , female/male; EDSS: Expanded Disability Status Scale; Ns, not significant

- CR tended to be decreased in POMS vs AOMS (p=0.05).
- Proportion of CI was 36% in POMS and 33% in AOMS (p=0.64).
- There was no difference in social and professional attainment between groups.
- In the whole sample, the multivariable analysis showed that the presence of CI was associated with
  - older age (OR=1.03 95%CI 1.01-1.07; p=0.039),
  - higher EDSS (OR=1.42 95%CI 1.15-1.76; p=0.001)
  - lower CR (OR=0.92 95%CI 0.89-0.96; p<0.001).
- Better social and professional attainments were associated with
  - CR (Beta 0.98-1.35, p<0.01)
  - male sex (Beta 7.79, p=0.005)
  - lower EDSS (Beta 0.40, p<0.001)

CONCLUSIONS

- In our sample, POMS was associated neither with higher prevalence of CI nor with lower occupational attainment in adulthood.
- CR is a key, potentially modifiable, protective factor for subject cognitive and socio-professional outcome. Concurrently, CR tends to be lower in POMS subjects.
- Our findings underscore the importance of interventions focusing on intellectual enrichment enhancement, particularly in the pediatric MS population, in order to achieve better cognitive, social and professional performances in adulthood.

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