Brain plasticity and cognitive reserve in Multiple Sclerosis

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Background

Cognitive impairment is frequent in Multiple Sclerosis (MS), affecting 45% to 70% of patients. It is mainly characterized by impairment in information processing speed, attention, memory and executive functions and is related to many different MRI measures of brain inflammation and degeneration. Cognitive reserve (CR) can mitigate the clinical deficits due to MS, similarly to what has been reported in Alzheimer disease (Sumowski et al., 2010). CR has classically been defined as the active attempt of the brain to cope with brain damage by using pre-existing cognitive processes, such as lifetime cultural enrichment and leisure activities. The functional MR correlates of cognitive reserve and their relation with neuropsychological deficits are not completely investigated.

Aim of the study: The current study aims to deeper investigate the functional correlates of CR and cognitive impairment in MS patients

Patients and methods

CR of a sample of 20 MS patients and 13 age and education matched individuals was measured by means of the Cognitive Reserve Index (CRI), evaluating patients' education, employment, hobbies and leisure activities (Nucci et al., 2011) and was related to their cognitive impairment, measured by the Cognitive Impairment Index (CII), a global index of cognitive deficit, obtained by summing the negative SD of patient's performance in each subtest of the Brief Repeatable Battery (Rao et al., 1991) and the Wisconsin Card Sorting Test (WCST) total errors and perseverative errors. In Table 1 are reported patients' and controls' clinical data as well as Expanded Disability Status Scale (EDSS), CII and CRI; in Table 2 patients' and Controls' tests' performance are presented.

An event related fMRI was performed in order to detect activations in brain areas during a n-back task. Comparison between MS and Controls and regression analyses were conducted on regions of interest, in order to find correlations between levels of activations and both CR and CII.

Tab.1 Clinical data of MS and Controls

	MS patients (n=20)	Controls (n=13)	t	p
Gender (♂/♀)	7/13	7/6	-	0.11
Age	51.1 (8.1)	50.5 (10.4)	0.18	0.85
Education (years)	10.7 (3.2)	12.8 (5.2)	-1.18	0.26
Disease Duration (years)	12 (8.9)	NA	-	-
EDSS	3.5 (2.5)	NA	-	.-
CII	-14.4 (9.1)	-7 (4.4)	-2.69	0.01
CRI	101.1(12.7)	104.4(12.8)	-0.76	0.46
MS treatment medication	4 interferon	NA	-	-
	2 copolimer	NA	-	-
	1 fingolimod	NA	-	-

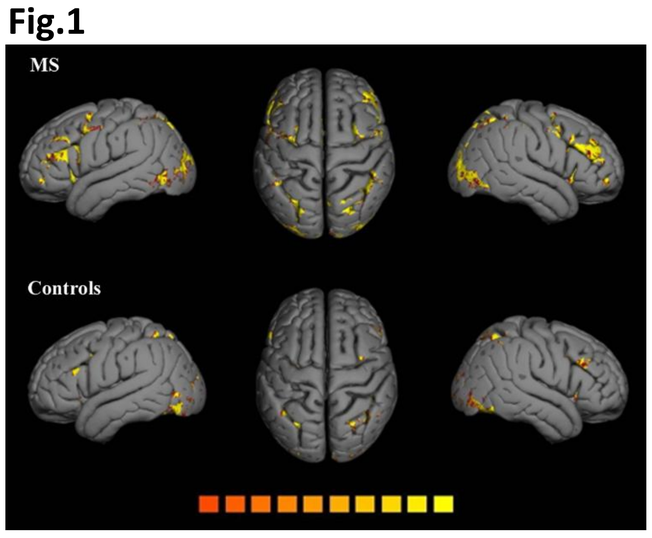
Tab.2 Patients' and Controls' test performance

	MS patients (n=20)	Controls (n=13)	T	p
SRT-LTS	29.3 (15.8)	41.9 (12.7)	-2.1	0.036
SRT -CLTR	20.5 (14)	32.9 (13.6)	-2.24	0.024
SRT -recall	6.4 (2.9)	8 (2.4)	-1.30	0.193
SPART	18.6 (4.5)	19.2 (5.2)	-0.30	0.762
SPART-recall	5.5 (1.9)	7 (1.7)	-2.18	0.027
SDMT	45.8 (16.2)	56.9 (11.3)	-1.91	0.056
PASAT3	31.7 (20.4)	46.3 (10.9)	-2.32	0.019
PASAT2	19.4 (15.9)	31.6 (10.8)	-1.98	0.047
WLG	23.7 (6.3)	28.2 (5.1)	-1.84	0.06
WCST % te	36.2 (22.9)	22.4 (11.5)	2.00	0.054
WCST % pe	22.5 (16.7)	11.8 (4.9)	1.57	0.11

Results

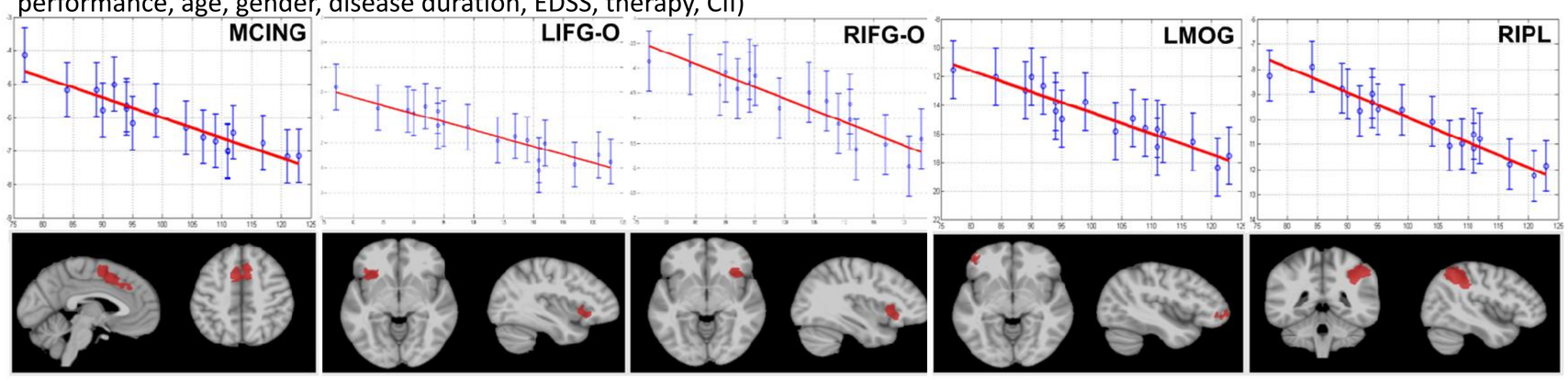
A - Significantly higher activation was found in MS patients compared to controls (Fig. 1)

Fig.1



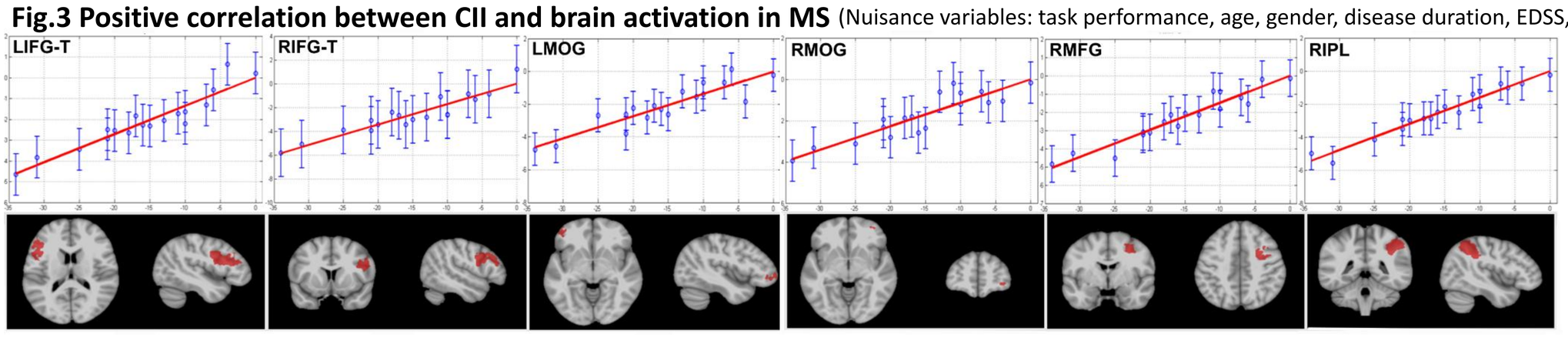
B - Regression analysis revealed: in MS a **negative correlation between CRI and brain activation** (i.e. the greater the CR the lower the brain activation) in the middle cingulum (r=.87), right (r=.83) and left (r=.85) inferior frontal gyrus, left medial orbital gyrus (r=.89) and right inferior parietal lobule (r=.93) (Fig.2). In Controls no significant correlations emerged.

Fig.2 Correlation between CRI and brain activation in MS (Nuisance variables: task performance, age, gender, disease duration, EDSS, therapy, CII)



C- On the contrary, in MS patients a **positive correlation was found between CII and brain activation** (i.e. the lower the CII, that is greater cognitive impairment, the smaller the brain activation) in several brain areas: the left (r=.89) and right (r=.84) inferior frontal gyrus, left and right (r=.78) medial orbital gyrus, right middle frontal gyrus (r=.89) e right inferior parietal lobule (r=.93) (Fig.3). In Controls the positive correlation was found in LIPL (r=.093) only.

Fig.3 Positive correlation between CII and brain activation in MS (Nuisance variables: task performance, age, gender, disease duration, EDSS, therapy, CRI)



Conclusions

These results might be explained by the greater brain functional efficiency in MS patients with higher cognitive reserve, shown by less need for brain activation. A failure in compensatory mechanisms due to increased disease related cognitive impairment of MS may be postulated for explaining the greater activation shown by impaired subjects.

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Nucci M et al.; Ageing Clin Exp Res (2012) 24(3): 218-26
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