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THE MODULATORY EFFECT OF COGNITIVE RESERVE ON THE CLINICAL OUTCOME OF PATIENTS WITH TRAUMATIC BRAIN INJURY: A VOXEL –BASED MORPHOMETRY STUDY

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Objective

It is becoming increasingly clear that, in several neurological conditions including Traumatic Brain Injury (TBI), there is a nonlinear relationship between the severity of patients' brain tissue damage and corresponding clinical symptoms. This has been shown in previous studies investigating the cross-sectional correlation between brain damage and symptoms in relation to cognitive reserve and seems to be particularly evident in those types of brain involvement which associate with disabilities. Cognitive reserve (CR) is a theoretical framework used to explain the different individual resilience to neurodegeneration and brain injury. Two different models of reserves have been proposed: (1) A passive model (brain reserve [BR]), which is based on quantifying brain size, neuronal amount, and number of synapses; and (2) an active model (cognitive reserve [CR]), which postulates the existence of brain mechanisms able to cope with cerebral damage. These mechanisms are believed to rely on pre-existing cognitive processes or to enlist compensatory processes. Although the precise process that underlie the positive effects of CR are not fully explored, the level of educational success that an individual may have attained before injury is considered an important indicator of CR and is accepted as a valid proxy measure. Evidence for the relationship between measures of CR and the development of cognitive problems and structural brain changes as a consequence of brain pathology has increasingly been documented in a variety of clinical contexts, including Alzheimer's disease, Parkinson's disease, multiple sclerosis. In the case of TBI, existing findings on the CR reported a better post injury outcome in the presence of greater CR, but the relationship between this variable and the brain volume loss and acquired lesions has not yet been studied .

Because formal education has been indicated as a positive predictor of age-associated cognitive decline in other neurological condition, we found it interesting to investigate the impact of formal education in modifying the relationship between GM tissue damage and clinical outcome, by using VBM in a cohort of patient with severe TBI in the subacute of phase of recovery. In particular, this study aimed at investigating the neurobiological correlates of cognitive reserve (CR) when modulating the clinical outcome of patients with traumatic brain injury (TBI). As previously shown in neurodegenerative diseases, we hypothesized here that changes in regional grey matter (GM) volumetrics might, at least partially reflect an effect of CR.

Methods

38 severe TBI (GCS ≤8 in the first 24h) patients in the subacute phase and 38 healthy subjects (HS) (Tab.1) underwent a 3T MRI brain scan. In all patients the functional clinical outcome was assessed using the Level of Cognitive Scale (LCF) and the Glasgow Outcome Scale (GOS). The traumatic lesion had to a size on FLAIR scans ranging between 153 and 311085 mm ^{3} . Patients were divided in two groups on the basis of their level of CR estimated by years of formal education: higher CR (HCR) and lower CR (LCR) (Tab.2). After outlining and removing macroscopic lesions, T1-weighted scans were used to perform voxel-based morphometry (VBM) analysis. We confined VBM analysis to the GM tissue that was spared by macroscopic damage in all patients. Between group comparisons (HCR, LCR and HS, respectively) in GM volumes were assessed using ANOVA model. Correlations between LCF/GOS and regional GM volumes were compared between HCR and LCR groups using a two-sample T-test. Results were accepted as significant at p values< 0.05 FWE corrected at cluster level.

	Patients group n=26	Healthy subjects n=38
age (years)	32.30 (12.65)	31.73 (11.85)
years of formal education	10.97 (3.26)	14,92 (2.5)
Gender (male/female)	22/4	25/13
coma duration (days)	22.5 (11.72)	-
LCF	5.15 (1.75)	-
GOS	2.9 (0.95)	-

Table 1. Demographic and clinical characteristics of the samples. Mean (SD)

	Patients grouping by formal education		
	HCR (n=13)	LCR (n=13)	*p value*
age (years)	33.07 (13.36)	31.53 (12.37)	0.79
years of formal education	13.9 (1.75)	8 (0)	0.00*
coma duration (days)	20.76 (7.94)	24.23 (14.70)	0.4
LCF	5.76 (1.01)	4.5 (2.14)	0.08
GOS	3.15 (0.3)	2.7 (1.3)	0.31

Table 2. Demographic and clinical characteristics of the HCR and LCR samples. Mean (SD)

Results

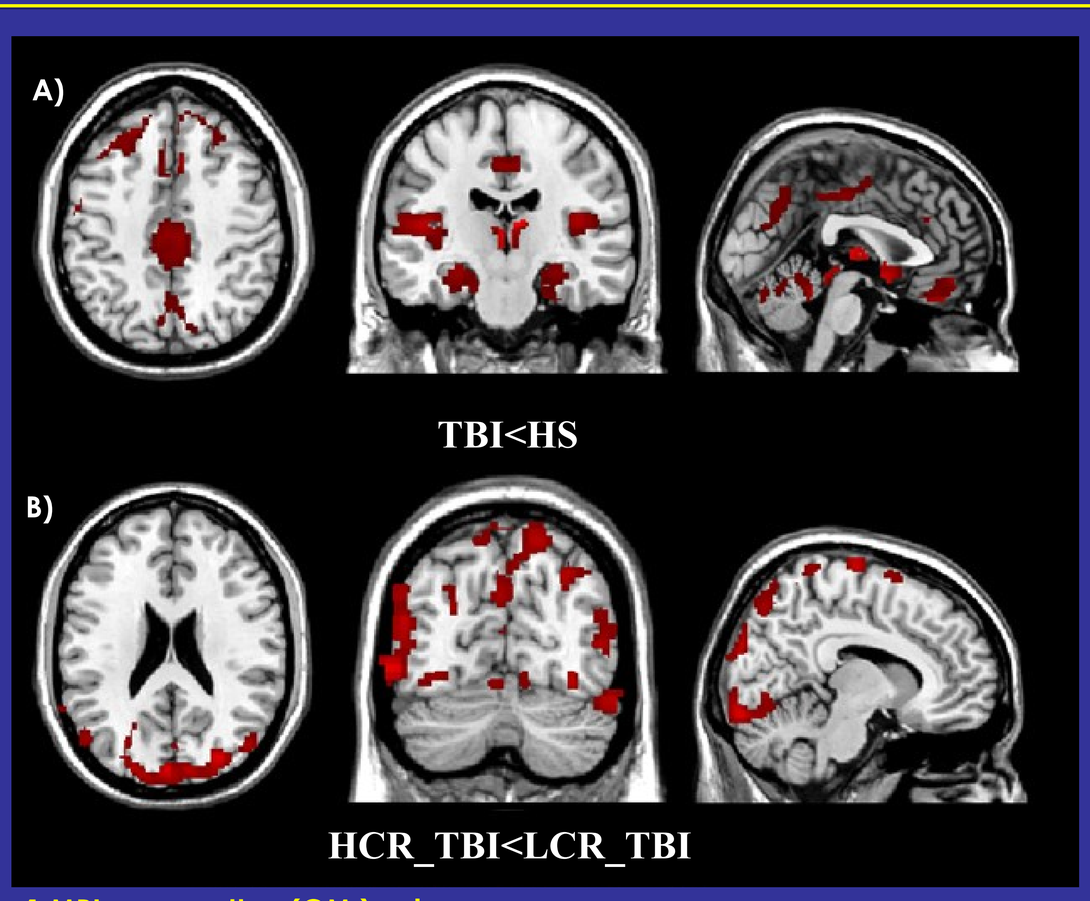
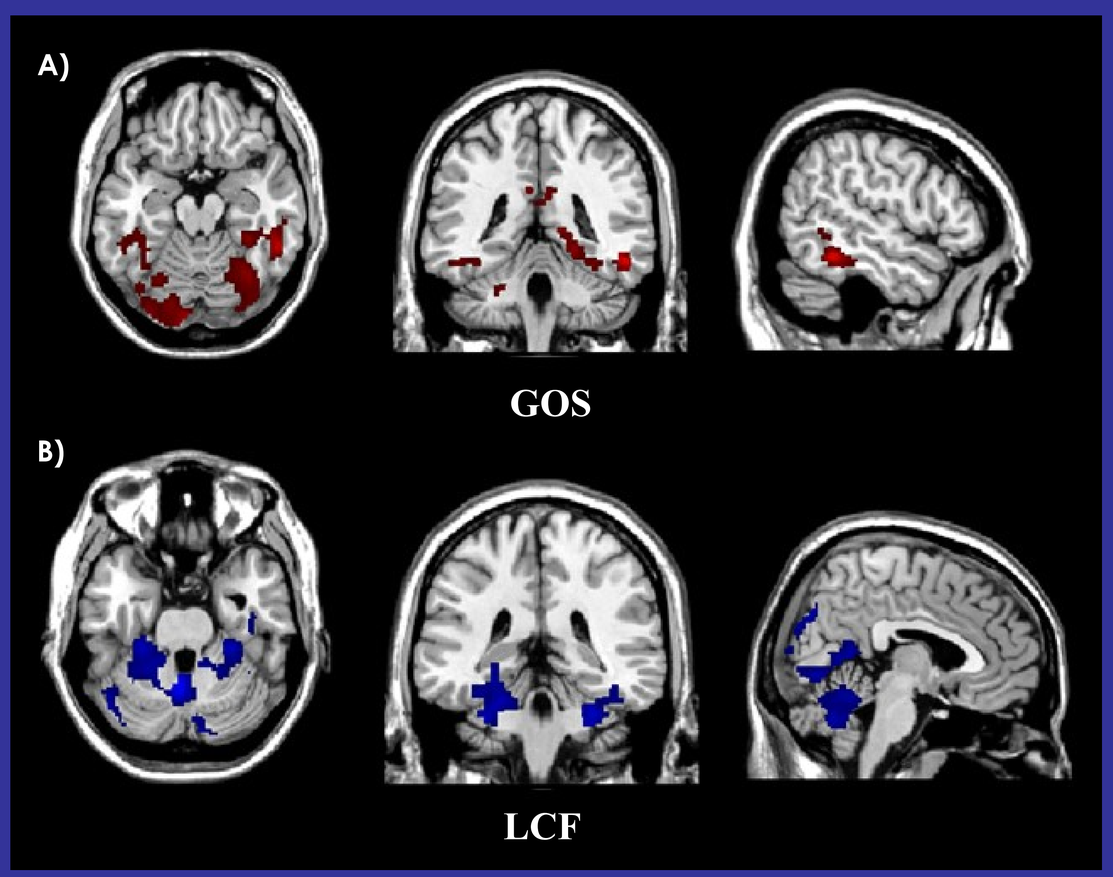


Fig.1 MRI grey matter (GM) volume
A)Regional changes in GM volumes between the TBI group and the Healthy Subjects group (HS).
Cross-sectional VBM comparison showed GM volume loss in the thalamus, Posterior Cingulate Cortex, Precuneus and Parieto-Occipital Lobe in TBI group compared to HS.
B) Regional changes in GM volumes between patients with TBI divided in those with an higher (HCR) and those with a lower educational level (LCR). HCR respect to LCR showed reduction in GM volume in precuneus, parieto-occipital associative areas.
The statistical images are overlaid onto a T1-weighted template image. Only statistical results (p<0.05 FWE cluster-level –corrected) are shown.

Fig.2 Grey matter loss correlated to clinical scores changes in TBI group (HCR>LCR).
One sample t- test analysis were employed to assess correlation between LCF and GOS scores and regional GM volumes in TBI HCR and LCR groups. The statistical images are overlaid onto a T1-weighted template image. Only statistical results (p<0.05 FWE cluster-level –corrected) are shown.
A) HCR, but not in LCR showed an association between GM volume loss mainly in the cerebellum and the inferior tempora gyrus and GOS score.
B) We found an association between GM loss in the cerebellum and LCF scores.



Conclusions

This is the first study that investigates the neurobiological correlates of CR in modulating the clinical outcome of patients suffering from TBI. Despite similar macroscopic lesions and clinical outcomes between groups, HCR patients showed an association between GM volumes in critical areas for cognition and their GOS and LCF scores. According to CR hypothesis , the findings of this study suggest that patients with higher CR withstand brain damage better than those with low CR (CR hypothesis).

References

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