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STRUCTURAL BRAIN ABNORMALITIES IN JOINT HYPERMOBILITY SYNDROME/EHLERS-DANLOS SYNDROME, HYPERMOBILITY TYPE. A PILOT STUDY.

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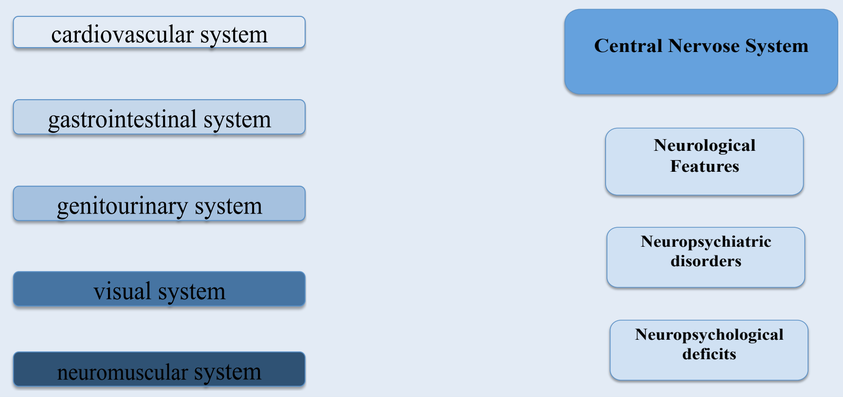
Introduction

The Ehlers-Danlos Syndrome, hypermobility type (EDS-HT), is a polyhedric condition. Whit Joint hypermobility syndrome (JHS), Ehlers-Danlos Syndrome, hypermobility type (EDS-HT), are two inherited connective tissue disorders mainly characterized by generalized joint hypermobility, complications of joint instability, minor skin changes, and musculoskeletal pain [1].
Currently, JHS and EDS-HT are considered as two rare clinically overlapping disorders. The JHS/EDS-HT is a multisystemic disease.

In this pilot study, we investigated the neuroanatomical features of patients with JHS/EDS-HT, using quantitative structural MRI. Principal objective of this study was to identify specific patterns of grey (GM) and white matter (WM) volumetric changes in a group of JHS/EDS-HT patients.

The clinical pictures distinguishable in patients with JHS/EDS-HT varies widely; this syndrome is defined as a disorder whit many faces that involves not only musculoskeletal and cutaneous systems, but also involving:

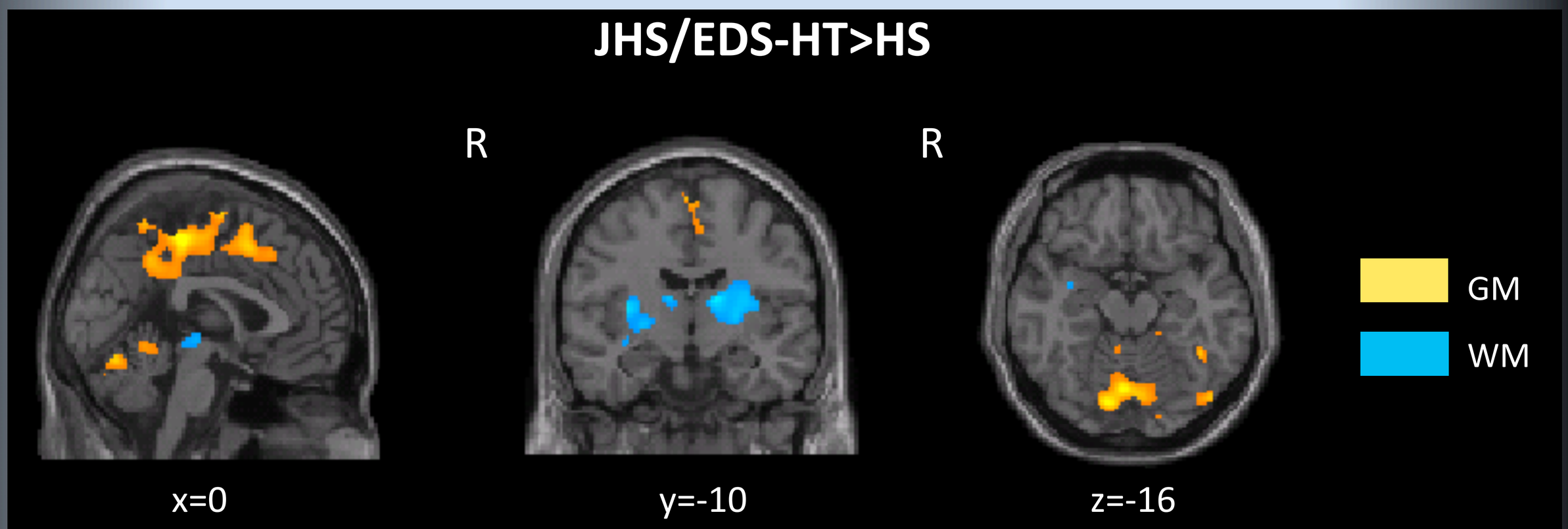


Cognitive Domain	Test
long-term memory	RAVLT
	Complex Rey's figure
short-term memory	Digit span forward
	Corsi block tapping
working memory	Digit span backward
visuo-constructive skills	Copy of geometric drawings
	Copy of complex Rey's figure
reasoning	Raven's coloured progressive matrices, MP47
attention	Visual search
executive functions	Phonological word fluency
	Trial Making Test [TMT part A, part B, part B-A]
	Stroop Color Word Interference Test
	Tower of London
	Wisconsin card Sorting Test

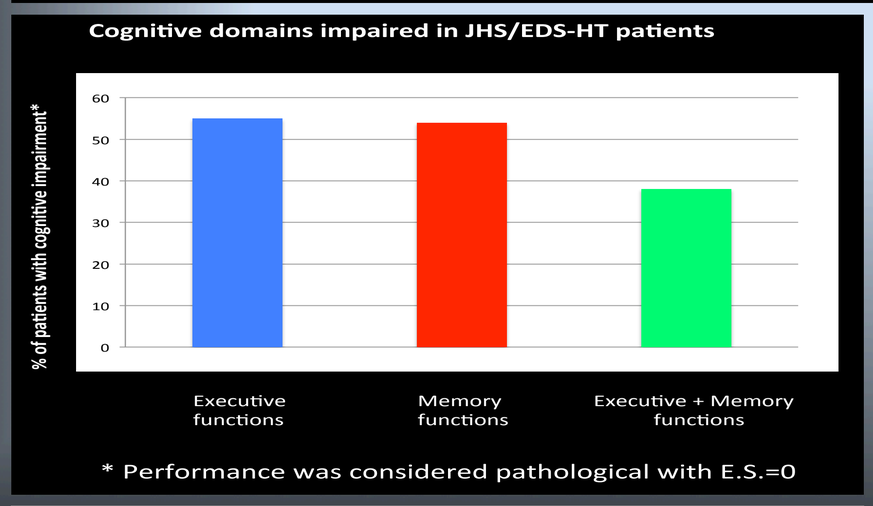
Neuropsychological tests used to define the neurocognitive profile of patients with JHS/EDS-HT. Patients' performances with equivalent score of zero, were considered pathological.

Methods

We recruited a cohort of 13 patients with clinical diagnosis of JHS/EDS-HT [2]. A group of 13 healthy controls matched for age, gender, and education level with our patients, were also enrolled. All participants underwent MRI at 3T. The MRI acquisition protocol included T2-weighted and fluid-attenuated inversion recovery (FLAIR) and T1-weighted volumes for volumetric measures. T1-weighted volumes were analysed according to an optimized protocol of voxel-based morphometry (VBM) to assess between-group differences in regional GM and WM volumes. To investigate patients' different cognitive domains (i.e., short and long term memory, attentive functions, logical reasoning, visuo-spatial and visuo-constructive abilities, and executive functions) we employed standardized tests, and we compared the scores reported by our patients with cut-off values derived by Italian normative data [3].



Areas of abnormal increased grey (GM) and white matter (WM) volumes in JHS/EDS-HT patients compared to control subjects group [*p<0.05 FWE corr.*].



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Results

When compared to controls, JHS/EDS-HT patients showed increased GM volumes in several brain areas, including cingulate and precuneus cortex, and the cerebellum (vermis crus I, II). Moreover, JHS/EDS-HT patients revealed a bilateral pattern of increased WM volumes in the basal ganglia, and thalami. From a neuropsychological viewpoint, all patients showed some abnormalities, ranging from isolated deficits of the executive (55% of cases) or memory functions (54%) to a multi-domain cognitive impairment (38%).

Conclusions

This pilot study showed, for the first time, that JHS/EDS-HT associates with cognitive impairment and structural brain abnormalities, involving both, the GM and WM. From a patho-physiological perspective, the regional increases of GM and WM volumes are likely due to phenomena of abnormal neuronal migration during brain development. Despite individual heterogeneity of symptoms, the distribution of these brain abnormalities might account for the cognitive profile we observed in our patient cohort. Future studies are needed to explore the different subtypes of JHS/EDS-HT.