Introduction: Myotonic Dystrophy type 1 (DM1) is the most common form of adult-onset autosomal dominant muscular dystrophy, due to an expansion of an unstable CTG-repeat in the 3'-untranslated region of a gene located on chromosome 19q13.3 encoding DMPLK protein (myotonic dystrophy protein kinase) \(^2\). The main clinical feature is myopathy, although CNS involvement has been demonstrated by clinical and neuroimaging studies. We aimed to evaluate both white matter (WM), using Tract Based Spatial Statistics (TBSS), and cortical alterations, using both Cortical Thickness analysis (CT) and Voxel-based Morphometry (VBM) after white matter lesion load refilling. \(^4\) We correlated TBSS, CT and VBM data with clinical and genetics severity.

Methods: 24 DM1 patients (age = 38.5±11.8 y, mean ± SD; 14 M), and 25 sex and age-matched healthy controls (38.5±11.3 y, 14 M) underwent a standardized brain MR protocol, including high resolution 3D FSPGR T1 and DTI (25 directions, b-value=900 mm\(^2\)/s) scans on a 1.5T GE scanner. Disability and neuromuscular impairment using a validated scale, corrected Mini-Mental State Examination (MMSE), and triplets expansion were assessed in all patients. Patients’ WM lesion load was calculated on FLAIR T2 images with the software JILIM.

In order to perform comparisons between patients and controls and correlations with clinical variables, for TBSS and VBM analysis, a voxelwise General Linear Model (GLM) was applied by using nonparametric permutation methods, while for CT analysis a vertex-by-vertex GLM was performed accounting for multiple comparisons by Monte Carlo simulation. Age and sex were added for TBSS analysis as nuisance regressors, while age, sex and total intracranial volume (TIV) for VBM and CT analysis.

Results: WM lesions load (17.2±27.5 cm\(^3\)) correlated with age at evaluation (r = 0.644; p = 0.003) and MMSE score (r = -0.487; p = 0.48). TBSS showed a widespread WM FA values reduction and MD, AD and RD values increase in DM1 patients compared to controls with a direct correlation between DTI metrics and cognitive (MMSE), neuropsychological (NP area), motor (motricity and myotonia area) and genetic data (triplets) (Fig. 1a). Cortical thickness reduction in the bilateral parietal-occipital cortex (Fig. 1b) and diffuse voxel-based gray matter reduction in both cortical and subcortical areas were found (Fig. 1c).

Conclusions

This multimodal MR study demonstrated diffuse white matter alterations in DM1 patients that correlated with cognitive performances, motor impairment and triplets expansion. Cortical thickness reduction was detected in the parietal-occipital cortex and gray matter volume loss in cortical (frontal, parietal, occipital, temporal, insular and cingulate cortices) and sub-cortical regions (hippocampus, thalamus, putamen and caudate nuclei).

References