Are white matter's changes in DM1 brain related to anosognosia?

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Introduction

Myotonic dystrophy type 1 (DM1) is an autosomal dominant neuro-muscular disorder characterized by unstable cytosine-tymine-guanine (CTG) triplet expansion in chromosome 19. It is the most common muscular dystrophy with juvenile or adulthood onset. DM1 is associated with an extreme clinical variability, affecting various organs and the CNS. Cerebral involvement in DM1, consists of extended mental impairment, executive dysfunction and the presence of avoidant personality.
Disconnection of cortical regions by changes of the connectivity of white matter (WM) is a potential mechanism for cognitive dysfunction, and it seems to be correlated to cognitive impairment more than grey matter atrophy.
Imaging techniques allow to investigate white matter alterations and brain MRI might be used to measure WM lesions.
Anosognosia (Gk. "gnosis", knowledge; "nosos", disease) has been defined as "apparent unawareness, misinterpretation, or explicit denial of illness" or as well as impaired insight for behavioural and cognitive problems.

Objective

- To correlate neuroradiological changes with neuropsychological and psychological features, in particular anosognosia.
- To quantify MRI lesions by a visual quantitative score (ARWMC)

Methods

Patients: We analysed 27 genetically proven patients with DM1 (age: 47.1 ± 12.2 years; male/female: 19/8; disease duration: 19.4 ±9.4 years).
All patients were investigated by neuropsychological assessment, structured psychological interview, brain MRI. One patient refused MRI for claustrophobia.
CTG repeat expansion size was determined in all patients (mean ± SD: 652.5 ±525; range: 65-1909 repeats). Educational level was assessed as a combination sum of graduation and professional qualification (mean ± SD: 11.6 ± 2.9). The Muscular impairment Rating Scale was used to assessed severity of disease (Table I).

	DM1 patients
Number of patients	27
Age	41.07 ± 12.2
Sex (M/F)	19/8
CTG repeat lenght (range)	652.5 ± 525 (65 – 1909)
Educational level	11.6 ± 2.9
Duration of disease (years)	19.4 ± 9.4
Severity of disease (Muscular Impairment Rating Scale)	3.2 ± 0.8

Table I. Clinical characteristics of patients with DM1 (mean ± DS)

Psychological Testing: Cognitive and psychological functions were assessed in all patients using a comparative neuropsychological test battery. We applied AES (Apathy Evaluation Scale) and InQoL (Individualized Neuromuscular Quality of Life) questionnaire to assess the presence of anosognosia. All patient and their caregivers were submitted to these tests to determine the presence of anosognosia (R.L). Anosognosia was given with a different total score between patient's self referred score and caregiver's score. The psychological tests was done blindly to MRI.

Magnetic Resonance Imaging (MRI): We acquired all MRI data at the I.R.C.C.S. Fondazione Ospadale San Camillo di Venezia, Italy, using a Philips Achieva Intera 1.5 T scanner. A eight-channel head coil was used for signal reception. All patients underwent the same imaging protocol consisting of whole brain T1 weighted, T2 weighted and diffusion-weighted imaging using an in-house DTI sequence. The total study time was 45 min per subjects, and all images were obtained in a only one session. All images were controlled by a visual inspection and artefacts were excluded.

Grading of white matter hyperintensity: Age Related White Matter Changes (ARWMC) scale: In the ARWMC scale the degree of white matter changes is rated on a four-point scale (Table II). Rating was done on MRI images on a computer screen in T2-weighted images and FLAIR images. WM changes in MRI were defined as ill-definited hyperintensities ≥ 5 mm. Five different regions were rated in the right and left hemispheres separately: the frontal area, the parietal area, the occipital area and the temporal area. The grading within five regions ranged from 0 (no lesions) to 3 (diffuse lesions). All ratings were performed by only one rater (C.A.) in two different sessions in San Camillo Hospital.

White matter lasions	
0	No lesions
1	Focal lesions (≥ 5 mm)
2	Beginning confluence of lesions
3	Diffuse involvement of the entire region

Table II. The ARWMC rating scale for MRI

Results

Patients with DM1 have more frequent and characteristic lesions in fronto-temporal regions (figure 1).
In our study brain involvement in DM1 has been scored after acquiring neuroimaging. Our study revealed the presence of white matter lesions, mainly located within anterior temporal lobes and frontal lobes. The graphic shows the prevalence of focal lesion in frontal lobe, and almost absence of lesion in the parietal areas. There is presence of more prominent lesions, focal and initially confluent, in the temporal area (in both hemispheres). (Figure 2).
Anosognosia was present in 72% of patients, i.e. seventeen of twenty-seven patients showed anosognosia. (figure 3). The distribution of white matter lesions is shown in figure 4. Figure 5 shows that the major load was encountered in fronto-temporal region.

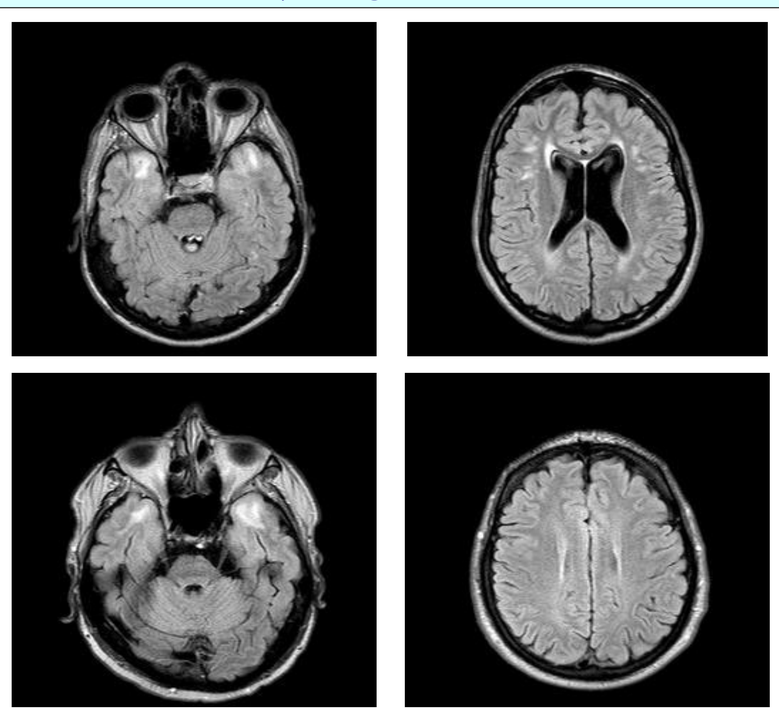

Fig. 1 Typical MRI abnormalities in DM1 patients. Diffuse sub cortical white matter changes are bilaterally observed in frontal and temporal regions.

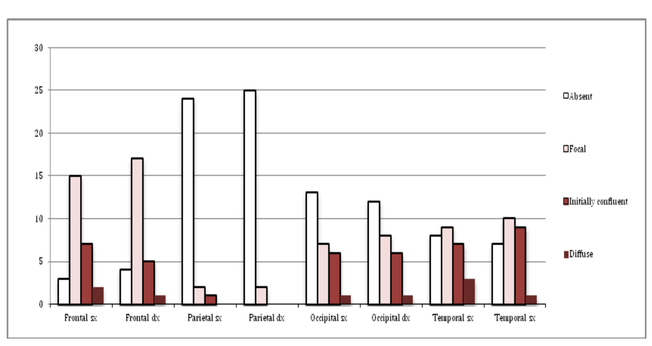

Fig. 2. Distribution of white matter lesions detected with ARWMC score, indicated in the graphic with different colours. Four areas are shown in both hemispheres.

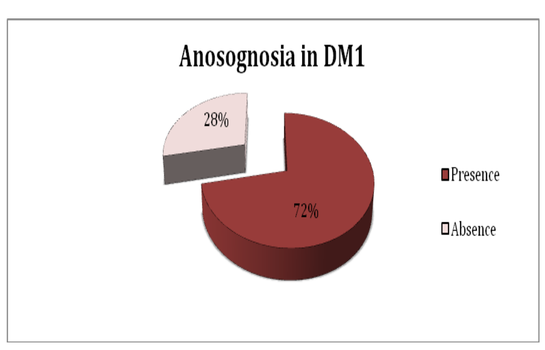

Fig. 3. Prevalence of anosognosia disorder in DM1 patients group

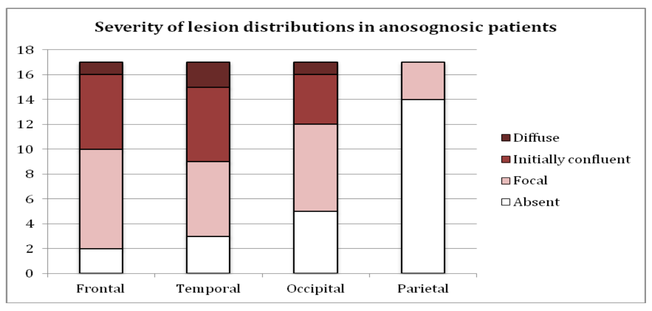

Fig. 5. The graphic shows that the major load in anosognosic patients are initially confluent or focal in fronto-temporal region

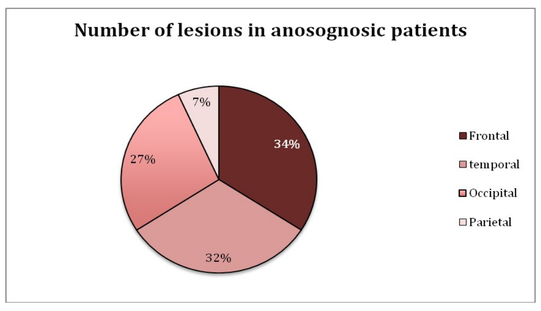

Fig. 4. Of 17 anosognosic patients, 34% have a frontal lesion and 32% have temporal lesions.

Conclusion

There is a prevalence of MRI lesions in 72% of patients, in our DM1 series.
The most frequent and typical white matter changes are in frontal and temporal localisation with diffuse and focal distribution. It is likely they are correlated not only with behavioural changes in DM1 but also with lack of recognition of their condition of anosognosia. Our findings are important in managing DM1 patients.

Refernces

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