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Differences in diffusion tensor imaging parameters of brain white matter tracts between patients with myotonic dystrophy type 1 and type 2 — a retrospective single-centre study

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ABSTRACT

Introduction. The main aim of our study was to compare diffusion tensor imaging (DTI) parameters in patients with myotonic dystrophy types 1 and 2 (DM1 and DM2).

Clinical rationale for the study. To ascertain whether DTI could be used to assess the integrity of white matter tracts in the brain and identify any abnormalities or disruptions in connectivity between different brain regions in patients with DM. By providing a more detailed understanding of the structural changes in the brain associated with DM, could DTI potentially be used to develop more effective treatments for the cognitive and neurological symptoms of the disorder?

Material and methods. We retrospectively compared MRI scans of 19 patients with DM1 to those of 23 healthy, matched controls, and of 16 patients with DM2 to those of 20 healthy, matched controls, and finally compared the DM1 and DM2 samples. Fraction anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD), and axial diffusivity (AD) values were assessed using Tract Based Spatial Statistics (TBSS).

Results. In patients with DM1, a statistically significant decrease in the values of the FA parameter was revealed in 45/48 white matter tracts compared to patients with DM2. There was no statistically significant decrease in the values of the FA parameter in patients with DM2 compared to DM1. The values of MD and RD were significantly higher in 47 tracts in DM1 patients compared to DM2 patients. AD values were significantly higher in all 48 tracts in DM1 patients compared to DM2 patients. There were no tracts with increased MD, AD, or RD values in DM2 patients compared to DM1.

Conclusions. Our results indicate diffuse disintegration of white matter pathways in DM patients, especially in the DM1 group. The damage to all types of fibres (association, commissural, and projection) may explain the diversity of clinical symptoms, which were more severe in the DM1 group of patients than in the DM2 group.

Clinical implications. DTI in patients with DM may help us to understand the neural mechanisms underlying brain involvement during the disease. In future, it may help to identify biomarkers for disease progression and treatment response.

Key words: myotonic dystrophy 1, myotonic dystrophy 2, diffusion tensor imaging, brain imaging

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Introduction

Myotonic dystrophy (DM) is the most common type of muscular dystrophy in adults, characterised by progressive muscle degeneration because of a genetic defect. The main, muscular symptoms in DM are accompanied by problems with the heart and digestive system, and hormonal disorders.

Two types of DM have been identified as taking different courses [1, 2].

In type 1 DM, the pathology results from a mutation in the gene encoding the protein kinase DPMK (dystrophia myotonica protein kinase) consisting of a CTG repeat expansion, while a CCTG repeat expansion in the zinc finger protein 9 gene (ZNF9) has been identified in myotonic dystrophy type 2 [3, 4]. Type 1 occurs in young patients, including children, and the severity of its course is associated with the amount of CTG repeat numbers [5]. In this type, the peripheral muscles and the voluntary (striated) muscles of the face are mainly affected, but also the independent muscles such as the heart and diaphragm, and the smooth muscles (gastrointestinal tract etc.) gradually also become involved.

Type 2 has a milder course with adult onset only, and it involves exclusively proximal voluntary muscles. This means that the disability may be greater even with less advanced disease [1, 2].

Central nervous system involvement occurs in both types of myotonic dystrophy, with type 1 being more severe and manifested by intellectual disability, reduced intelligence quotient (IQ), memory disorders, visual and hearing impairment, excessive daytime sleepiness, avoidant personality, and low self-esteem [6–10]. In type 2, the IQ is usually normal, while visual-spatial disturbances, excessive daytime sleepiness, and a profile of psychological disorders (avoidant personality) occur at a similar frequency as in DM1, but to a lesser degree [7, 11, 12].

The pathogenesis of the involvement of the central nervous system is not fully understood. Some authors include myotonic dystrophies in the subgroup of neurodegenerative diseases called tauopathies because of intraneuronal accumulation of abnormally modified microtubule-associated tau protein in the brains of patients with DM [13–19].

Magnetic resonance imaging (MRI) is the best tool to assess the brain in patients with DM. In both types of DM, the lesions mainly concern white matter and are visible on T2/FLAIR images as white matter hyperintense lesions (WMHL). In type 1, they are located in the frontal and temporal lobes, while in type 2 they are located in the periventricular white matter in the frontal and parieto-occipital lobes. Characteristics for type 1 lesions located in the anterior part of the temporal lobes (anterotemporal white matter lesion, ATWML) are usually not observed in type 2 [20].

Novel techniques, such as T2 relaxometry, magnetisation transfer (MT), voxel-based morphometry (VBM), and diffusion tensor imaging (DTI), can specifically and more deeply analyse structural changes within white matter (WM), and they demonstrate extensive white matter involvement compared to morphological images [5]. In particular, DTI, based on a region of interest (ROI) approach or with the use of more advanced tract-based spatial statistics (TBSS), proves that white matter abnormalities in DM patients are more frequent and pronounced than has been previously suggested [21]. The DTI technique has been effectively used to assess the integrity of white matter pathways in various physiological conditions, including the learning process, memory, and brain ageing, as well as in numerous neurological diseases. It is also valuable in preoperative planning prior to the removal of a brain tumour or a cavernous haemangioma [22, 23].

The aim of our study was to compare DTI parameters in patients with DM1 and DM2 to those of sex- and age-matched healthy controls, and between DM1 and DM2 patients. Afterwards, we checked how the DTI parameters in DM1 and DM2 patients correlated with the duration of the disease.

Clinical rationale for the study

A study on DTI in patients with DM could provide important insights into the neural mechanisms underlying CNS involvement in DM. Specifically, DTI could be used to assess the integrity of white matter tracts in the brain and identify any abnormalities or disruptions in connectivity between different brain regions in patients with DM.

By providing a more detailed understanding of the structural changes in the brain associated with DM, DTI could potentially be used to develop more effective treatments for the cognitive and neurological symptoms of the disorder. Additionally, DTI might serve as a useful biomarker for monitoring disease progression and treatment response in patients with DM.

Material and methods

Participants

From the 37 MRIs performed in DM patients in the 2nd Department of Clinical Radiology of the Medical University of Warsaw, Poland between 2009 and 2020, we selected 35 adolescents for further analysis.

Only patients with a genetically confirmed mutation were included in the study, and they were assigned to the appropriate DM group (DM1 or DM2) according to the mutation type. The other inclusion criteria were: a good quality DTI examination using at least 20 diffusion directions, the absence of focal lesions other than those typical of DM on morphological sequences, and age above 18 years. Patients without a DTI sequence or with poor image quality were excluded from the study.

We formed two control groups (HC1 and HC2) age- and sex-matched to each type of DM.

It has been demonstrated that there are age-related changes in the integrity of white matter tracts, which are manifested

by alterations in DTI parameters. In older patients, there is a decrease in FA and an increase in MD [24].

Because of the significant difference in age between DM1 and DM2 patients, we introduced two age-matched control groups, to avoid the effect of age-related changes on the DTI parameters.

The control groups consisted of healthy subjects without any neurological symptoms and with no pathological lesions within the brain on structural MR images.

All procedures were performed in compliance with the Declaration of Helsinki. Ethical approval was not required due to the retrospective study design.

Data acquisition

All patients and controls underwent an MRI examination on a 1.5-T scanner (Avanto, Siemens, Erlangen, Germany). A 12-channel head coil was used. The examination protocol started from morphological sequences: 2D T2 TSE in transverse, coronal, and sagittal planes, 2D T2 FLAIR, 2D T1 SE, DWI in transverse plane, and sagittal 3D MPR T1 followed by DTI sequence. Detailed image parameters are included in Supplementary Table 1.

The DTI protocol differed depending on the date of acquisition: we started with a single-shell 20-direction protocol (between 2009 and 2011), but from 2012 we upgraded this to 30 directions of diffusion. Only six patients with DM1 and three with DM2 underwent a DTI study with the use of 20 directions of diffusion. The remaining 26 patients (13 with DM1 and 13 with DM2) underwent a DTI study with a 30-direction protocol. Accordingly, in the control group for DM1 there were six examinations with 20 directions and three in the control group for DM2.

Diffusion-weighted images were collected using a gradient echo-planar imaging sequence (echo time TE = 86 ms, repetition time TR = 3,300 ms with the two diffusion weightings of b1 = 0 s/mm^2 and b2 = 1,000 s/mm^2, voxel size 1.8 × 1.8 × 5 mm, FoV 230 mm, 25 slices per volume). The acquisition time was 5.05 minutes for 20 directions and 6.59 minutes for 30 directions of diffusion.

All patients and controls gave written informed consent for the examination and for the use of MRI data for research.

Data processing

Fractional anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD), and axial diffusivity (AD) maps were calculated after susceptibility-induced distortion, eddy current, and head motion correction. DTI data was corrected by applying an affine transformation of each image to the B0 image using the Oxford FSL toolkit (http://www.fmrib.ox.ac.uk/fsl/fdt/index.html). For each voxel, tensor eigenvectors and corresponding eigenvalues as well as FA, MD, RD, and AD values were computed.

FA, MD, RD, and AD maps were then fed into standard TBSS skeletonisation using the Oxford FSL toolkit [25].

Next, each subject's FA, MD, RD, and AD data was projected onto FMRIB58_FA standard space (which is in the same space as the MNI152 standard space). Each subject's FA and maps were visually inspected for the quality of this registration. Then, TBSS skeletons were segmented according to the Johns Hopkins ICBM-DTI-81 atlas containing 48 white matter tracts. For each region, average FA, MD, RD, and AD values were extracted.

Statistical analysis

Averaged FA, MD, RD, and AD values in the ROI were compared between DM1 and HC1, DM2 and HC2, and finally between DM1 and DM2 samples using a standard non-parametric test. False discovery rate (FDR) p values were computed using Freeman & Lane (1983) (default in FSL GLM randomize) to control the FDR for multiple tests.

To detect between-group differences, we used a cluster-based thresholding, a voxel-wise thresholding, and a threshold-free cluster enhancement approach (TFCE). We have presented the results based on threshold-free cluster enhancement, which provides better sensitivity and richer and more interpretable output than cluster-based and voxel-wise thresholding [26].

The number of permutations was set to 5,000. P-value < 0.05 after family-wise error corrections for multiple comparisons was applied.

The effect associated with the diffusion-encoding gradient directions (20 or 30 in this case) was included as an additional regressor in the statistical model. In this way, any differences due to the number of diffusion-encoding directions were regressed out during statistical comparisons.

FA, MD, RD, and AD values in white matter tracts were compared with disease duration.

Results

Patients

The final patient cohort consisted of 19 patients with DM1 (aged 20 to 57 years; mean age 39; median age 39; female/male 4/15) and 16 patients with DM2 (aged 20 to 64 years; mean age 50; median age 54; female/male 12/4).

There was a statistically significant difference in the mean age between the two groups of patients at p = 0.009.

Out of 53 people, we selected 23 healthy individuals aged between 19 and 57 years (median age 39; female/male 4/19) as the control group for DM1, and 20 healthy individuals aged 22 to 62 (median age 54; female/male 12/8) for comparison to DM2.

Diffusion tensor imaging — comparing myotonic dystrophy type 1 to healthy controls 1

Supplementary Table 2 sets out the detailed differences between DM1 and HC1 in all tested white matter tracts. Compared to HC1, patients with DM1 had reduced FA and

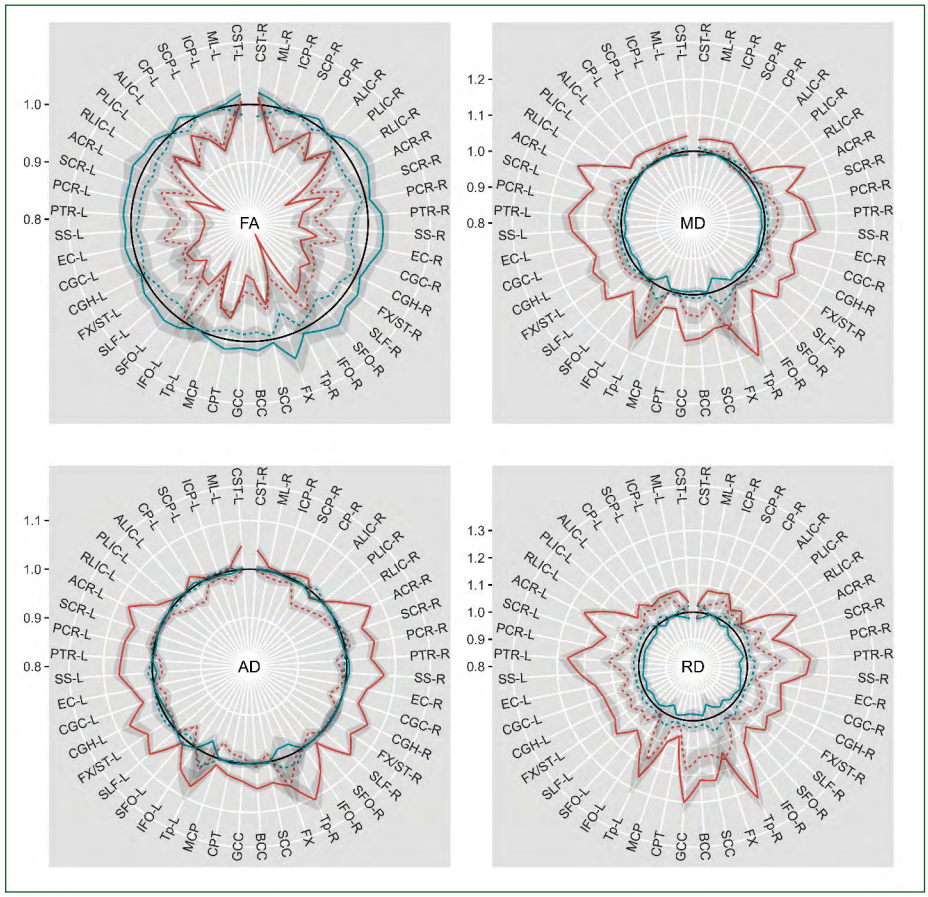

Figure 1. Radar chart illustrating in detail differences between DM type 1 and type 2 patients for all regions altogether. Solid red line — DM1 patient; solid blue line — HC1; dashed red line — DM2 patient; dashed blue line — HC2; grey fields — standard error; solid black line is average value of two control groups. Thus, average of two control groups is reference value, and is 1. MCP — middle cerebellar peduncle; CPT — pontine crossing tract; GCC — genu of corpus callosum; BCC — body of corpus callosum; SCC — splenium of corpus callosum; FX — fornix; CST-R — corticospinal tract r; CST-L — corticospinal tract l; ML-R — medial lemniscus r; ML-L — medial lemniscus l; ICP-R — inferior cerebellar peduncle r; ICP-L — inferior cerebellar peduncle l; SCP-R — superior cerebellar peduncle r; SCP-L — superior cerebellar peduncle l; CP-R — cerebral peduncle r; CP-L — cerebral peduncle l; ALIC-R — anterior limb of internal capsule r; ALIC-L — anterior limb of internal capsule l; PLIC-R — posterior limb of internal capsule r; PLIC-L — posterior limb of internal capsule l; RLIC-R — retrolenticular part of internal capsule r; RLIC-L — retrolenticular part of internal capsule l; ACR-R — anterior corona radiata r; ACR-L — anterior corona radiata l; SCR-R — superior corona radiata r; SCR-L — superior corona radiata l; PCR-R — posterior corona radiata r; PCR-L — posterior corona radiata l; PTR-R — posterior thalamic radiation (include optic radiation) r; PTR-L — posterior thalamic radiation (include optic radiation) l; SS-R — sagittal stratum (including inferior longitudinal fasciculus and inferior fronto-occipital fasciculus) r; SS-L — sagittal stratum (including inferior longitudinal fasciculus and inferior fronto-occipital fasciculus) l; EC-R — external capsule r; EC-L — external capsule l; CGC-R — cingulum (cingulate gyrus) r; CGC-L — cingulum (cingulate gyrus) l; CGH-R — cingulum (hippocampus) r; CGH-L — cingulum (hippocampus) l; FX/ST-R — fornix (cres)/ /Stria terminalis (cannot be resolved with current resolution) r; FX/ST-L — fornix (cres)/Stria terminalis (cannot be resolved with current resolution) l; SLF-R — superior longitudinal fasciculus r; SLF-L — superior longitudinal fasciculus l; SFO-R — superior fronto-occipital fasciculus (could be a part of anterior internal capsule) r; SFO-L — superior fronto-occipital fasciculus (could be a part of anterior internal capsule) l; IFO-R — uncinate fasciculus r; IFO-L — uncinate fasciculus l; Tp-R — tapetum r; Tp-L — tapetum l

increased MD and RD in all white matter tracts. Increased AD was found in 45 white matter tracts.

There was no increase in FA and no decrease in MD, AD, or RD parameters in any white matter tracts in the HC1 group compared to DM1 patients.

Detailed results are set out in Figure 1 and Table 1.

Diffusion tensor imaging — comparing myotonic dystrophy type 2 to healthy controls 2

Supplementary Table 3 sets out detailed differences between DM2 and HC2 in all tested white matter tracts. Compared to HC2, patients with DM2 had decreased FA values revealed in 41 white matter tracts. No decrease in FA values

Table 1. Differences of FA, AD, RD, and parameter in white matter tracts between tested groups. Red indicates tracts with decreased values and green indicates tracts with increased values

FA				
vs.	**DM1**	**DM2**	**HC1**	**HC2**
DM1	–	0	0	–
DM2	45	–	–	0
HC1	48	–	–	–
HC2	–	41	–	–
AD				
vs.	**DM1**	**DM2**	**HC1**	**HC2**
DM1	–	0	0	–
DM2	45	–	–	7
HC1	44	–	–	–
HC2	–	0	–	–
RD				
vs.	**DM1**	**DM2**	**HC1**	**HC2**
DM1	–	0	0	–
DM2	47	–	–	
HC1	48	–	–	–
HC2	–	17	–	–
MD				
vs.	**DM1**	**DM2**	**HC1**	**HC2**
DM1	–	0	0	–
DM2	47	–	–	0
HC1	48	–	–	–
HC2	–	0	–	–

in any white matter tract was demonstrated in subjects from the HC2 group compared to DM2.

No statistically significant difference in the value of the MD parameter was found between DM2 and HC2 or between HC2 and DM2 in any white matter tract.

RD was higher in 28 out of 48 white matter tracts and AD was lower in 9 out of 48 white matter tracts in DM2 patients compared to HC2.

Detailed results are set out in Figure 1 and Table 1.

Diffusion tensor imaging — comparing myotonic dystrophy types 1 and 2

Table 2 sets out detailed differences in all tested white matter tracts. In patients with DM1, a statistically significant decrease in the values of the FA parameter was revealed in 45 out of 48 white matter tracts compared to patients with DM2.

There was no statistically significant decrease in the values of FA parameter in patients with DM2 compared to DM1.

The values of MD and RD were significantly higher in 47 tracts in DM1 patients compared to DM2 patients. AD values were significantly higher in all 48 tracts in DM1 patients compared to DM2 patients.

There were no tracts with increased MD, AD, or RD values in DM2 patients compared to DM1.

Detailed results are set out in Figures 1 and 2 and in Table 1.

Diffusion tensor imaging — considering disease duration

The mean age at disease onset in patients with DM1 was 27.2 years, and the mean disease duration was 11.3 years (range 2–34). In DM2 patients, the mean age at disease onset was 35.1 years, and the mean disease duration was 13.4 years (range 1–33). The disease duration in patients with DM1 and DM2 was compared to the average FA, MD, RD, and AD values of white matter tracts. Only the FA parameter in DM2 patients showed negative correlation with the duration of the disease. A statistically significant FA decrease was noted in 7 out of 48 white matter tracts; namely, body of corpus callosum, splenium of corpus callosum, left cerebral peduncle, left anterior limb of internal capsule, left posterior limb of internal capsule, left superior corona radiata, and superior fronto-occipital fasciculus.

We did not find any relationship between DTI parameters and disease duration in the group of DM1 patients.

Discussion

This study presents an analysis of white matter tract integrity in patients with DM1 and DM2 based on DTI parameters using TBSS — an unbiased automated technique in which whole-brain-based voxel-wise comparison between groups can be made. We used two different control groups matched for both types of dystrophy first in order to eliminate the age differences that occur between patients with types 1 and 2.

We found a statistically significant reduction of FA in all 48 analysed white matter tracts in DM1 patients compared to HC1 and in 41 of 48 white matter tracts in DM2 patients compared to HC2. A comparison of patients with DM1 and DM2 revealed lower values of the FA parameter in the DM1 group in 45 out of 48 white matter tracts. The values of MD, RD, and AD were significantly higher in 47, 47, and 48 tracts respectively in DM1 patients compared to DM2 patients.

These results indicate diffuse disintegration of white matter pathways in DM patients, especially in the DM1 group. The damage to all type of fibres (association, commissural, and projection) may explain the diversity of clinical symptoms, which were more severe in the DM1 group of patients compared to the DM2 group.

When comparing disease duration, there was no statistically significant relationship with FA, MD, RD, or AD in DM1 patients, whereas in 7/48 DM2 patients, white matter tracts showed an FA decrease. This may suggest that the damage in DM1 is more severe from the onset of the disease, while in DM2 the process is gradual, which perhaps makes it possible to find a way to delay or stop progression of the disease.

Table 2. Differences in 48 white matter tracts according to Johns Hopkins ICBM-DTI-81 atlas

No.	White matter tract	TBSS TFCE FA DM2 > DM1 (p-value)	TBSS TFCE MD DM1 > DM2 (p-value)	TBSS TFCE AD DM1 > DM2 (p-value)	TBSS TFCE RD DM1 > DM2 (p-value)
1	Middle cerebellar peduncle	p = 0.0008	p < 0.0002	p < 0.0002	p < 0.0002
2	Pontine crossing tract	p = 0.0008	p < 0.0002	p < 0.0002	p < 0.0002
3	Genu of corpus callosum	p = 0.0004	p < 0.0002	p < 0.0002	p < 0.0002
4	Body of corpus callosum	p = 0.0004	p < 0.0002	p < 0.0002	p < 0.0002
5	Splenium of corpus callosum	p = 0.0004	p < 0.0002	p < 0.0002	p < 0.0002
6	Fornix	p = 0.0048	p < 0.0002	p < 0.0002	p < 0.0002
7	Corticospinal tract R	p = 0.0008	p < 0.0002	p < 0.0002	p < 0.0002
8	Corticospinal tract L	p = 0.0008	p < 0.0002	p < 0.0002	p < 0.0002
9	Medial lemniscus R	p = 0.0022	p < 0.0002	p < 0.0002	p < 0.0002
10	Medial lemniscus L	–	p < 0.0002	p < 0.0002	p = 0.0004
11	Inferior cerebellar peduncle R	p = 0.0024	p < 0.0002	p = 0.0156	p < 0.0002
12	Inferior cerebellar peduncle L	–	p < 0.0002	p = 0.0156	p = 0.0004
13	Superior cerebellar peduncle R	p = 0.0008	p < 0.0002	p < 0.0002	p < 0.0002
14	Superior cerebellar peduncle L	p = 0.0008	p < 0.0002	p < 0.0002	p < 0.0002
15	Cerebral peduncle R	p = 0.0006	p < 0.0002	p < 0.0002	p < 0.0002
16	Cerebral peduncle L	p = 0.0006	p < 0.0002	p < 0.0002	p < 0.0002
17	Anterior limb of internal capsule R	p = 0.0006	p < 0.0002	p < 0.0002	p < 0.0002
18	Anterior limb of internal capsule L	p = 0.0004	p < 0.0002	p < 0.0002	p < 0.0002
19	Posterior limb of internal capsule R	p = 0.0008	p < 0.0002	p < 0.0002	p < 0.0002
20	Posterior limb of internal capsule L	p = 0.0004	p < 0.0002	p < 0.0002	p < 0.0002
21	Retrolenticular part of internal capsule R	p = 0.0006	p < 0.0002	p < 0.0002	p < 0.0002
22	Retrolenticular part of internal capsule L	p = 0.0004	p < 0.0002	p < 0.0002	p < 0.0002
23	Anterior corona radiata R	p = 0.0006	p < 0.0002	p < 0.0002	p < 0.0002
24	Anterior corona radiata L	p = 0.0004	p < 0.0002	p < 0.0002	p < 0.0002
25	Superior corona radiata R	p = 0.0006	p < 0.0002	p < 0.0002	p < 0.0002
26	Superior corona radiata L	p = 0.0004	p < 0.0002	p < 0.0002	p < 0.0002
27	Posterior corona radiata R	p = 0.0006	p < 0.0002	p < 0.0002	p < 0.0002
28	Posterior corona radiata L	p = 0.0004	p < 0.0002	p < 0.0002	p < 0.0002
29	Posterior thalamic radiation R	p = 0.0006	p < 0.0002	p < 0.0002	p < 0.0002
30	Posterior thalamic radiation L	p = 0.0004	p < 0.0002	p < 0.0002	p < 0.0002
31	Sagittal stratum R	p = 0.0006	p < 0.0002	p < 0.0002	p < 0.0002
32	Sagittal stratum L	p = 0.0004	p < 0.0002	p < 0.0002	p < 0.0002
33	External capsule R	p = 0.0006	p < 0.0002	p < 0.0002	p < 0.0002
34	External capsule L	p = 0.0004	p < 0.0002	p < 0.0002	p < 0.0002
35	Cingulum (cingulate gyrus) R	p = 0.0012	p < 0.0002	p < 0.0002	p < 0.0002
36	Cingulum (cingulate gyrus) L	–	p < 0.0002	p < 0.0002	p < 0.0002
37	Cingulum (hippocampus) R	p = 0.0004	p < 0.0002	p < 0.0002	p < 0.0002
38	Cingulum (hippocampus) L	p = 0.0372	p < 0.0002	p < 0.0002	p < 0.0002
39	Fornix (cres) R	p = 0.0006	p < 0.0002	p < 0.0002	p < 0.0002
40	Fornix (cres) L	p = 0.0004	p < 0.0002	p < 0.0002	p < 0.0002
41	Superior longitudinal fasciculus R	p = 0.0006	p < 0.0002	p < 0.0002	p < 0.0002
42	Superior longitudinal fasciculus L	p = 0.0004	p < 0.0002	p < 0.0002	p < 0.0002
43	Superior fronto-occipital fasciculus R	p = 0.0006	p < 0.0002	p < 0.0002	p < 0.0002
44	Superior fronto-occipital fasciculus L	p = 0.0006	p < 0.0002	p < 0.0002	p < 0.0002
45	Uncinate fasciculus R	p = 0.0006	p < 0.0002	p < 0.0002	p < 0.0002
46	Uncinate fasciculus L	p = 0.0004	p < 0.0002	p < 0.0002	p < 0.0002
47	Tapetum R	p = 0.0006	p < 0.0002	p < 0.0002	p < 0.0002
48	Tapetum L	p = 0.0380	–	p = 0.0156	–

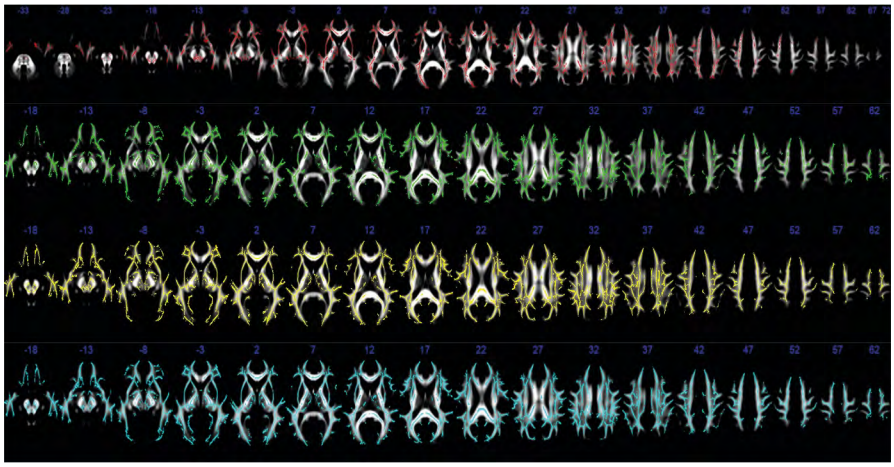

Figure 2. Tract-based spatial statistics map using TFCE approach: white matter tracts with FA reduction in DM1 patients compared to DM2 patients (shown in red), white matter tracts with AD (shown in green), RD (shown in yellow) and MD (shown in blue) increase in DM1 patients compared to DM2 patients

There have only been a few studies on DTI in DM1 patients [21, 27–29], with only two publications to date comparing DTI parameters between both types of DM and between DM patients and a control group.

Minnerop et al. [5] analysed 22 patients with DM1, 22 with DM2, and 22 age- and sex-matched healthy controls. Using TBSS, they compared DM1 to the controls, DM2 to the controls, and both types to each other. According to their results, association fibres throughout the whole brain, limbic system fibre tracts, the callosal body, and projection fibres were affected in DM1 and DM2; however, white matter occupation in DM1 was more prominent than in DM2, which is in accordance with our findings. According to Minnerop et al. [5], central motor pathways were exclusively impaired in DM1, whereas in our study, in DM1 in both corticospinal tracts, FA increased; a decrease in MD, AD, and RD was noted only in DM2, and a decrease of FA in the left corticospinal tracts was found.

The group of patients studied by Franc et al. [30] consisted of only 20 subjects (five for each group i.e. congenital-onset DM1, adult-onset DM1, DM2, and controls). A significant difference in FA in each brain compartment among all four groups ($p < 0.003$) was revealed, and pair-wise significant differences of mean FA within the brain compartments were observed between each of the three DM groups compared to controls. However, DM1 patients had significantly lower FA than controls in the inferior frontal, supra-callosal, and occipital regions ($p < 0.05$), while DM2 and controls did not. An ROI-based approach was applied to analyse DTI parameters, which is a less accurate, and more observer-dependent, method compared to the TBSS technique we used in our analysis.

A limitation of our study is the lack of clinical information and correlation with muscle status and intellectual assessment, as well as with psychological tests and the length of sleep during the day. Knowing that the severity of the course is associated with the amount of CTG repeat numbers, it would also be interesting to correlate genetics with the DTI characteristics of white matter tracts. Therefore, we are planning in our further study to focus on finding the association between diffusion parameters and physical and mental status, as well as with genetics results, to better understand the pathogenetic processes of central system involvement.

Conclusions

DTI allows us to better understand the neural mechanisms underlying CNS involvement in myotonic dystrophy. The application of DTI may help to identify biomarkers for disease progression and treatment response, and ultimately to develop more effective treatments for the cognitive and neurological symptoms of DM.

Article information

Data availability statement: *Data available upon request from the authors.*
Ethics statement: *All procedures were performed in compliance with the Declaration of Helsinki. Ethical approval was not required due to the retrospective study design.*
Authors' contributions: *EM — study conception and design, draft manuscript preparation; TW — analysis and interpretation of results, statistics; JdeM, KJ — data collection; MW — editing; AK-P, MG — critical article revision for important intellectual content; AL — data collection, revision of article and approval of publication. All authors approved final version of manuscript.*
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Supplementary materials: *Supplementary materials are available on journal's website.*

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