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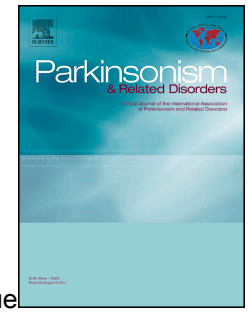

Analysis of diffusion tensor parameters in spinocerebellar ataxia type 3 and type 10 patients

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Analysis of diffusion tensor parameters in spinocerebellar ataxia type 3 and type 10 patients

Running head – DTI parameters in SCA3 and SCA10

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Abstract

Introduction – There is a dearth of studies of spinocerebellar ataxias (SCAs) and diffusion tensor magnetic resonance imaging (DTI). **Objective –** To analyze changes observed in DTI parameters and correlate these to clinical findings in SCA3 and SCA10 patients. **Methods –** SCA3 (n=19) and SCA10 (n=18) patients were compared with a similar number of controls and assessed clinically and with the scale for the assessment and rating of ataxia (SARA) before undergoing the same MRI protocol. TRACULA (TRActs Constrained by UnderLying Anatomy) software was used to analyze the DTI metrics FA, AD, RD and MD. **Results –** More white matter fiber tracts with changes in diffusivity were found in SCA3 patients than in SCA10 patients. There was a reduction in AD in altered fiber tracts in SCA3 and a greater increase in RD in SCA10. In the SCA3 patients, FA was reduced in the corticospinal tract (CST) and inferior longitudinal fasciculus (ILF), but this was not observed in the SCA10 patients. SARA score was correlated with DTI findings in SCA3 but not in SCA10. **Conclusion –** Changes were observed in DTI for both SCA3 and SCA10 but were more widespread in SCA3. Our finding of myelin-sheath changes in SCA10 and secondary axonal changes in SCA3 may reflect the more rapid, aggressive clinical course of SCA3.

Keywords: Spinocerebellar ataxias; Machado-Joseph disease; ataxins; neuroimaging; magnetic resonance image; diffusion tensor imaging; FreeSurfer.

Introduction

Spinocerebellar ataxias (SCAs) are a heterogeneous group of ataxic disorders characterized by progressive cerebellar dysfunction [1,2]. They have an autosomal dominant inheritance pattern, and the current classification is based on the specific gene found to be associated with each disorder. At least 48 genetic loci, and 36 causal genes, have been described to date [1,2]. SCA3 is the most common type worldwide, also in Brazil, and present with a widely varying phenotype that includes oculomotor changes, pyramidal manifestations, movement disorders, peripheral neuropathy and cognitive decline [3]. SCA10 represents a rare type of SCA in the world, however, in some areas of the southern of Brazil it is the second most common type of SCA. It manifests as slow progressive cerebellar ataxia, dysarthria, dysphagia, epilepsy and other non-motor symptoms such as dysautonomia, cognitive dysfunction, psychiatric disorders, chronic pain and sleep disorders. Although SCA10 is typically associated with epilepsy, this is not a common finding in patients in southern Brazil [4,5].

Neuroimaging (NI) can be useful when assessing SCAs as it facilitates diagnosis, although a perfect correlation between the results of NI and genotype has not yet been established [6]. The main NI findings in SCA3 patients are significant loss of gray matter (GM) and white matter (WM) in the cerebellar hemispheres, lateral thalamus and brain stem, and there is a strong correlation between WM volume loss and disease severity [6]. NI findings in SCA10 patients indicate predominantly cerebellar atrophy (both hemispheric and of the cerebellar vermis) [7]. A few studies have investigated brain diffusion tensor magnetic resonance imaging (DTI) parameters in these types of SCA, and the main findings for SCA3 were greater atrophy and diffusivity of the pontine tegmentum compared with patients with the cerebellar variant of multiple system atrophy (MSA-C). This atrophy and mean diffusivity (MD) of the ventral pontocerebellar tract, as well as the reduction in fractional anisotropy (FA) in the cerebellum and brain stem, have been correlated with disease severity [8,9]. Another study found a strong correlation between SARA score and WM integrity as indicated by the FA of the brain stem, frontal thalamus and left cerebellar hemisphere [10]. These studies found greater FA and MD at the expense of RD, suggesting that the pathological changes had their origin in the myelin sheath [8-10]. To the authors' knowledge, there are to date no DTI studies of SCA10.

The present study sought to analyze changes in WM parameters acquired with DTI in SCA3 and SCA10 patients.

Methods

A cross-sectional research was conducted in the Ataxia Outpatient Clinic, Movement Disorders Unit, Neurology Service, Hospital de Clínicas, Federal University of Paraná, from April 2014 to April 2016.

Selection of patients and controls

The sample consisted of nineteen SCA3 and eighteen SCA10 patients were recruited among patients being followed at the Ataxia Outpatient Clinic. All the patients had a clinical and genetic diagnosis and were aged 18 years or older. Patients who were not able to have an MRI scan, for example those who had a psychiatric comorbidity such as claustrophobia or a psychosis, were pregnant, had a serious cognitive disability or had a non-MRI compatible implant, were excluded. Patients with neurological diseases whose results could lead to dubious interpretation of the images were also excluded, as were patients with other conditions such as alcoholism and systemic malignant neoplasms or patients for whom MRI was contraindicated or who were using medications with potentially neurotoxic effects (particularly to the cerebellum). Patients whose results could not be used because they moved during the examination or because of artifacts that could prevent satisfactory analysis of the results were asked to repeat the examination and were excluded if this was not possible. The study was approved by the HC/UFPR Committee for Ethics in Research (CAAE no. 47417015.9.0000.0096), and all gave informed written consent.

SCA3 and SCA10 control groups (n=19 and n=18, respectively) were formed from healthy volunteers in the community paired for age and sex.

Clinical Assessment and Neuroimaging

Demographic variables (age, sex), clinical variables (age of onset, clinical history, results of neurological examination) and molecular findings (expansion length) were collected with a standardized protocol used in the Movement Disorders Unit, Neurology Service, at the Hospital de Clínicas, Federal University of Paraná. Disease severity was assessed for all patients with a Portuguese version of SARA, the scale for the assessment and rating of ataxia, validated for Brazil. The SARA scale extends from 0 (no ataxia) to 40 (severe ataxia) [11,12].

Patients and controls underwent the same neuroimaging protocol in a Siemens 3T MRI MAGNETOM Skyra scanner (Siemens Healthcare, Erlangen, Germany) with a 16-channel head coil. The following three-dimensional Magnetization Prepared Rapid Acquisition Gradient Echo (MP-RAGE) anatomical sequence was used for segmentation in FreeSurfer: 176 sagittal slices, field of view 256 mm, slice thickness 1 mm, echo time 3.36 ms, repetition time 2530 ms, inversion time 1100 ms, bandwidth 200 Hz/pixel, flip angle 7º. Diffusion-tensor images were acquired with the following parameters: tensor – 30 orientations; 64 axial slices; thickness – 2 mm; FOV – 256 mm; TR – 8600 ms; TE – 95 ms. The WM parameters acquired by DTI were fractional anisotropy (FA), axial diffusivity (AD), radial diffusivity (RD) and mean diffusivity (MD) [13].

Images with a medium-to-high number of movement artifacts were excluded before processing. Some patients had to repeat the examinations on different days so that an image suitable for processing could be obtained.

TRACULA (TRActs Constrained by UnderLying Anatomy) was used to reconstruct WM tracts automatically from the DTI results. This tool uses probabilistic tractography with anatomical priors derived from an atlas and combined with patient segmentation in FreeSurfer, avoiding the need for user interaction, with stablished external validation (stable version 5.3 http://surfer.nmr.mgh.harvard.edu/) [14-16]. Tract processing was inspected visually, and when reconstruction errors were observed tracts with errors were corrected with a script in TRACULA. The diffusion metrics (FA, AD, RD and MD) automatically obtained by the software in this way were tabulated in Excel for analysis and comparison.

The DTI parameters are closely related to underlying cell physiology as well as tissue microstructure, as shown by well-established researches. The fractional anisotropy (FA) is a diffusion directionality index within a voxel and the medium diffusivity (MD) measures the overall diffusivity in tissue, thus they have been used as sensitive measure of water diffusion in the biological tissue, reflecting *in vivo* microstructural properties/alterations of WM (i.e., both decreased FA or increased MD), although less specific to the type of alteration. On the other hand, the axial diffusivity (AD), which measures the diffusion along fiber bundles, and the radial diffusivity (RD), which measures the diffusion orthogonal to fiber bundles, have been related with axonal density and membrane permeability, respectively, when decreased AD or increased RD. These techniques allow to gather information about structural brain connectivity, and

early detection of pathological alterations, and could be used as tracking of subtle changes in the follow-up examinations and clinical trials [17].

Two tracts along the medial line and eight bilateral tracts were analyzed, giving a total of eighteen tracts: forceps major (FMa) and forceps minor (Fmi); and cingulate fasciculus (CF), cingulum angular bundle (CAB), anterior thalamic radiation (ATR), uncinate fasciculus (UNF), corticospinal tract (CST), inferior longitudinal fasciculus (ILF), superior longitudinal fasciculus (SLF), the latter divided into temporal and parietal segments (SLFt and SLFp), respectively.

Statistical Analysis

The results are presented as mean, median, minimum, maximum and standard deviation for quantitative variables, and frequency and percentage for categorical variables. The Shapiro-Wilk test was used to determine whether the variables had a normal distribution. Student's t-test or the non-parametric Mann-Whitney test were used to compare quantitative variables between groups, and the chi-square test with Yates correction and the Fisher exact test were used to compare categorical variables between groups. The Spearman correlation coefficient was used to measure the association between two quantitative variables; the magnitude of the correlation was classified as follows: [0.00 to ±0.30] – biologically insignificant, [±0.31 to ±0.50] – weak, [±0.51 to ±0.70] – moderate, [±0.71 to ±0.89] – strong, [±0.91 to ±1.00] – very strong. The data were tabulated in Microsoft Excel 365 and analyzed in *Free Statistics Software* (v 1.2.1) [18].

Results

Mean age of the SCA3 patients when the assessment was carried out was 44.80 ± 12.50 years, while the mean age at symptom onset was 34.21 ± 8.38 years. In the SCA10 group, the corresponding figures were 46.43 ± 8.04 and 32.72 ± 8.51 years, respectively (Table 1).

All the patients presented with gait ataxia, and other signs were also common to both patient groups: limb ataxia (10 vs. 11), dysarthria (17 vs. 17) and nystagmus (14 vs. 10). Some signs were present in statistically significant numbers in SCA3 compared with SCA10: bulging eyes (5 vs. 0, $p = 0.019$), vertical ophthalmoplegia (12 vs. 1; $p = 0.008$) and horizontal ophthalmoplegia (8 vs. 1; $p = 0.018$). While three patients in the SCA3 group presented with spasticity and another four with hyperreflexia, none of the

patients in the SCA10 group presented with any signs of pyramidal tract dysfunction. The patients in the SCA10 group did not present with epilepsy.

Significant positive correlations were observed between disease duration and SARA score for both groups: the correlation was strong in the SCA3 group ($\rho = 0.872$; $p = 0.000$) and moderate in the SCA10 group ($\rho = 0.590$; $p = 0.005$). The data for the DTI metrics (FA, AD, MD, RD) are summarized in Figures 1A and 1B for SCA3 and SCA10, respectively. The complete data are available in Tables S1 and S2 (Supplementary Material).

For both SCA3 and SCA10, a reduction in FA was observed in the FMa, FMi and right CF and SLFp, and an increase in MD and RD in the left SLFp, SLFt and UNF (Figure 1). For SCA3, there was a reduction in FA in the left ATR and SLFt and in the CST and ILF on both sides, and a reduction in AD in the FMa and right CST. An increase in MD was observed in the FMi and left ILF, and in RD in the right ATR. For SCA10, there was a reduction in FA in the right SLFt and in AD in the right SLFp, as well as an increase in MD in the left ILF and in RD in the FMa and right CF (Figure 1).

For tracts that showed abnormalities, correlations were found between clinical data and molecular findings (expansion length) (Table 2). There was a correlation between CST and age, disease duration and SARA score in SCA3 patients but no correlation with spasticity.

Discussion

In this study we analyzed supratentorial WM tracts and showed, for the first time, tract abnormalities in SCA10 patients that were generally suggestive of lesions of the myelin sheath. More heterogeneous, diffuse changes were found in SCA3 patients, including involvement of both myelin and axons. There was no statistically significant correlation between the number of nucleotide repeats in either SCA10 (ATTCTn) or SCA3 (CAGn) and lesion type (axonal or demyelinating), disease duration, location of the lesions or clinical severity. Our finding of either a weak correlation or no correlation between CAGn and changes in brain structures agree with the findings of previous studies that used the same imaging techniques but studied infratentorial structures [8,10,19].

In SCA3 there was a greater correlation between tract involvement and clinical and molecular characteristics than in SCA10. The involvement of the corticospinal tract in SCA3 was striking and included bilateral FA reduction and right DA reduction,

which correlated with duration, suggesting a secondary axonal involvement in the right hemisphere. Previous studies that used DTI in SCA3 patients have pointed to increased RD, suggestive of demyelination, as the main pathological mechanism [8-10,19-22]. Only Guimarães et al. (2013) [8] found increased AD, indicating axonal loss, in the brain stem, cerebellum and thalamus. D'Abreu et al. (2009) [23], using MRI spectroscopy, found axonal lesions and lesions of the myelinated sheath in SCA3 patients. We also found that in the right corticospinal tract there was a moderate correlation with disease duration (in AD) and SARA score (in FA) and a weak correlation with age (in FA), suggesting that axonal involvement may be secondary to disease progression. This is in agreement with previous neuropathological studies in which the ataxin-3 protein was present in the form of axonal inclusions in areas with and without neurodegeneration [24]. There was corticospinal tract involvement asymmetry. This finding may be related to hemispheric dominance, which, in a certain way, progressed more importantly on the right side with axonal involvement correlated with the disease duration. Previous study using DTI also showed this CST asymmetry, although not related to hemisphere dominance [25].

In SCA10 we found less tracts with reduction of AD. Both decreased FA and AD on the right and increased MD and RD on the left, suggesting the presence of axonal and myelin-sheath involvement, in the parietal segment of the SLF, were correlated with the size of the expansion (MD and RD). Because both SCA3 and SCA10 have similar durations in this study, it is reasonable to suggest that SCA3 may lead to earlier AD reduction changes than SCA10, which would also explain the slower, less aggressive clinical course of the latter. As non-cerebellar signs, symptoms and imaging changes are uncommon in SCA10 patients, pathological changes in the brain may also be unremarkable. A study with histopathological sections found subtle changes in WM, but not the cerebral cortex, in SCA10 patients [26]. Identification of the underlying pathology is important to enable treatment strategies to be chosen but is not possible with a physical examination or conventional imaging, as these do not show non-cerebellar signs and symptoms in SCA10 [6,17]. Identification of differences with a quantitative DTI approach can provide the basis for clinical studies in which pre- and post-treatment findings are compared or SCAs are compared with each other or with other neurodegenerative diseases in order to increase our understanding of the pathophysiological progression of this group of disorders [17].

We found more diffuse and more significant changes in SCA3 than in SCA10, corroborating the difference in the clinical picture, which is more exuberant in patients with SCA3. Interestingly, although SCA10 has a purer cerebellar phenotype, in patients with this type of SCA we also found changes in supratentorial tracts not directly connected to the cerebellum. These findings, probably related to non-motor symptoms, were not generally correlated with disease duration, suggesting that the changes occur at the same time as cerebellar changes rather than secondary to them.

In SCA3, limb ataxia was correlated with decreased FA for the FMi and truncal ataxia with decreased AD for the FMa, suggesting that supratentorial commissural matter tracts are involved in the symptoms of ataxia. The frontal lobe is known to be involved in gait ataxia in a presentation known as frontal ataxia, which is characterized by the absence of poor coordination and the presence of disequilibrium and impaired postural reflexes, which can progress to the more severe gait apraxia, with astasia-abasia and magnetic gait [27]. The circuit involved in these presentations includes the fronto-ponto-cerebellar or cerebello-thalamo-cortical pathways [28]. Impaired frontal cortex activation and perfusion in SCA3 prior to ataxia and correlated with disease severity is well known [6,28], and in advanced stages of the disease mild frontal atrophy can be observed [6]. Now, our data suggests a participation of frontal connectives in the appendicular coordination in SCA patients, differently from frontal ataxia which is related to gait ataxia. Although in SCA10 limb ataxia was correlated with increased MD for the ILF, we did not observe any clinical association.

Pyramidal tract dysfunction was found in seven patients in the SCA3 group (spasticity and/or hyperreflexia) but in none of the SCA10 patients. We found corticospinal changes bilaterally in SCA3 but not in SCA10. These clinical findings were correlated with the DTI findings for some tracts (decreased FA for the CF and the ILF, and decreased FA, and increased MD and RD for the SLFt) for SCA3 but not for the CST, which was correlated with SARA score, age (decreased FA for both) and disease duration (decreased AD). In addition, we performed a subgroup analysis within the SCA3, comparing patients with and without spasticity and / or hyperreflexia, and their corticospinal tracts were not different between groups, for all evaluated parameters ($p > 0.112$). Our results suggest that it is important that future studies attempt to identify lesions in the CSTs to help differentiate between different SCA3 subphenotypes or their different clinical courses or even to select patients for studies into motor neuron impairment.

There was no correlation between SARA scores and WM tract alterations in our SCA10 patients. In the SCA3 patients, however, SARA score was correlated with DTI findings for the CST and SLFt. Previous studies using DTI [9,10,19,20] have shown that multiple extracerebellar structures play a role in disease severity. In two volumetric studies of SCA10 patients, the results for volume reduction in the thalamus were discordant [29,30]. Interestingly, our SCA10 patients neither showed any changes in ATR nor presented with epilepsy, unlike the SCA10 patients in a Mexican study, who showed a reduction in thalamic volume and presented with epilepsy. Analysis of the thalamus and the associated tracts could potentially be useful when assessing SCA10 patients to help identify those who may develop epilepsy during the course of the disease [29-31]. In SCA3, the thalamus was the supratentorial structure that had the most striking changes in previous studies in both neuroimaging and anatomic pathology investigations [6,24], corroborating our finding of bilateral changes in the ATR.

A recent study in which population was the same of the present study focused on volumetric changes on neuroimaging and showed more widespread alterations in SCA3 than in SCA10 group. Also, in that study the CAGn was more negative correlated with the thalamus and subcortical GM volumes for SCA3 patients [31]. For supratentorial structures, volume abnormalities were found in total GM cortex, thalamus, pallidum and putamen for SCA3, but only in lateral ventricles and pallidum for SCA10. Although supratentorial WM abnormalities was not find in both groups for that study, in the present study we found tract alterations in DTI parameters, which suggests a subjacent pathology with independent progression of the cerebellar involvement. In SCA3 group, thinner structures in the left pars triangularis of the inferior frontal gyrus was found in that previous research, which may correspond to the altered left temporal region of the superior longitudinal fasciculus in this study [31]. Besides the same altered tract was found in the SCA10 group, without the corresponding thinner cortical abnormality. Thus, it suggested that the present abnormalities in the WM tracts are independent of the cortical and volumetric abnormalities, and both information be interpreted together with cerebellar data should to explain the complexity of these diseases.

Reduction in FA the CF in SCA10 were correlated with disease duration in patients without apparent impaired cognitive functions and with nystagmus. This tract is involved in motor control, emotional, cognitive and behavioral functions and has been implicated in emotional and behavioral deficits, reduced spontaneous behavior, intentional saccade, executive dysfunction and depression [32]. Although nystagmus

was weakly correlated with the right CF, neither axial or appendicular ataxia, nor dysarthria were correlated with this tract. Other fascicles that showed changes in our SCA3 and SCA10 patients may also be associated with behavioral and cognitive changes. A major limitation of our analysis of the results was that we did not carry out a formal cognitive assessment of the patients. We also did not perform motor control assessment, but patients did not show frontal release signs, once both might represent cingulate dysfunction [33]. Furthermore, we excluded patients with severe psychiatric or cognitive impairments that would have prevented them from having an imaging examination; in other words, we excluded patients with more severe subcortical changes from our analysis, which may be considered a bias.

The small sample of patients available in rare diseases is a limitation for this type of study, which constrain the statistical power of the data. Further multicenter researches are necessary to confirm the results herein obtained.

In conclusion, changes in relation to the controls were observed in DTI for both SCA3 and SCA10 but were more diffuse, heterogeneous and clinically correlated in SCA3. While in SCA10 the changes we observed were characteristic of breakdown of the myelin sheath, in SCA3 we also observed secondary axonal changes, possibly reflecting the more rapid, aggressive clinical course of SCA3. This study has shown that DTI can be used in a comparative analysis of the clinical course of SCAs.

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FIGURE 1. BRAIN WHITE MATTER TRACTS IN SCA3 AND SCA10 PATIENTS: CHANGES COMPARED WITH CONTROLS

SOURCE: The authors (2020).
NOTES: The colors indicate the type of axonal lesion (reduced AD – dark gray ■) or demyelinating lesion (increased RD – light gray ■) or nonspecific change (reduced FA and/or increased MD – gray ■). Unaltered tracts are not colored.
LEGENDS: 1 – forceps minor (FMi); 2 – forceps major (FMa); 3 – anterior thalamic radiation (ATR); 4 – parietal region of the superior longitudinal fasciculus (SLFp); 5 – temporal region of the superior longitudinal fasciculus (SLFt); 6 – inferior longitudinal fasciculus (ILF); 7 – cingulate fasciculus (CF); 8 – uncinate fasciculus (UNF); 9 – cingulum angular bundle (CAB); 10 –corticospinal tract (CST); R – right; L – left; SCA3 – Spinocerebellar ataxia type 3; SCA10 – Spinocerebellar ataxia type 10.

TABLE 1. DEMOGRAPHIC, GENETIC AND CLINICAL CHARACTERISTICS OF THE GROUP.

Characteristic	**SCA3**			**SCA10**		
	Patients (n=19)	Controls (n=19)	p	Patients (n=19)	Controls (n=19)	p
Gender						
Male	11	11	1	9	9	1
Female	8	8		9	9	
Age (in years)						
Male	47.98±10.25	46.17±9.42	0.67	48.88±7.5	48.25±8.38	0.87
Female	43.36±15.40	43.37±15.04	1	45.95±9.95	47.34±10.66	0.77
Total	44.80±12.50	44.99±11.8	0.395	47.34±8.76	47.77±8.39	0.442
						0.362*
Age of onset[a]	34.21±8.38	NA	NA	33.78±8.14	NA	0.876*
Disease duration[b]	11.89±7.45	NA	NA	11.32±10.20	NA	0.847*
SARA score	5 a 25	NA	NA	1 a 17	NA	
Mean	14.13±5.60	NA	NA	8.08±4.19	NA	**0.0007***
Median	13	NA	NA	8.25	NA	
Expansions	62 a 78	NA	NA	1400 a 2300	NA	NA
Mean	71.7±5.00	NA	NA	1918±185.16	NA	NA
Median	74	NA	NA	1970	NA	NA

SOURCE: The authors (2020).

LEGEND: [a] – Age at onset of symptoms (in years); [b] – Disease duration (in years); [c] – expansions in the affected allele (CAGn for SCA3; ATTCTn for SCA10); SD = standard deviation; NA = not applicable; *p** = between SCA3 and SCA10; SARA = Scale for the Assessment and Rating of Ataxia.

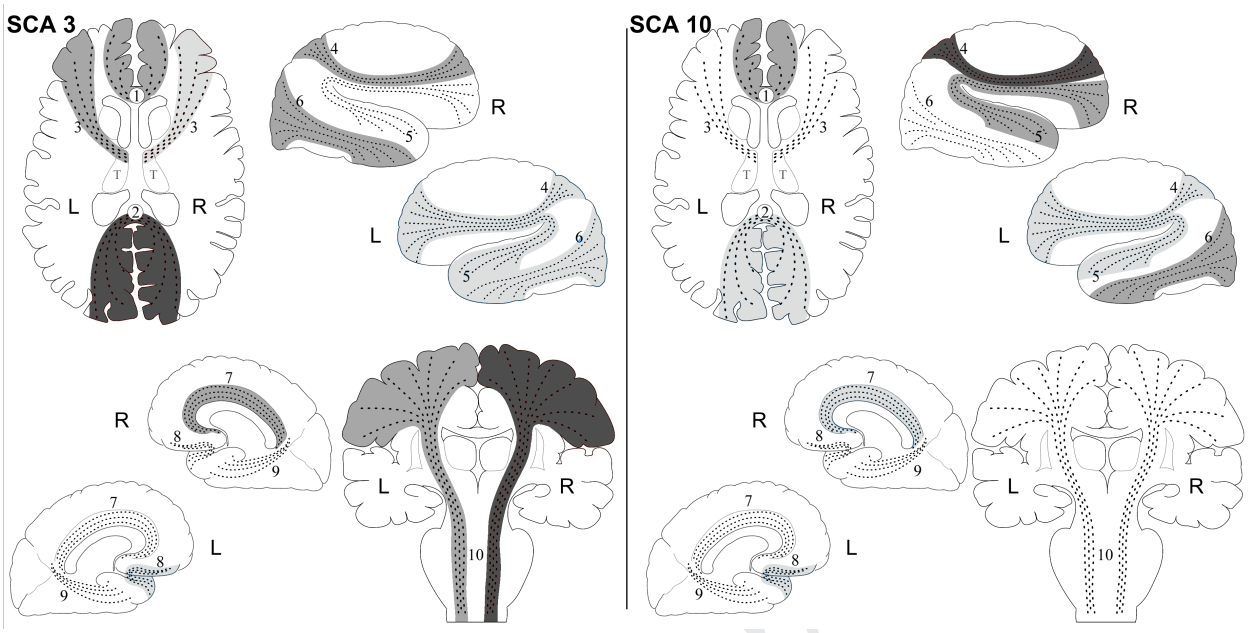
TABLE 2. CORRELATION BETWEEN ALTERED CLINICAL TRACTS (PATIENTS VS. CONTROLS) AND CLINICAL DATA AND MOLECULAR FINDINGS.

Data	SCA3			SCA10		
	Coef.	**Tract**	**Correlation***	**Coef.**	**Tract**	**Correlation***
Age	FA	FMI	ρ = -0.67; p = 0.001	–	–	–
		CST R	ρ = -0.50; p = 0.030	–	–	–
Duration	AD	CST D	ρ = -0.55; p = 0.013	FA	CF R	ρ = 0.64; p = 0.004
Age of onset	FA	FMI	ρ = -0.59; p = 0.008	–	–	–
SARA score	FA	CST L	ρ = -0.47; p = 0.045	–	–	–
		CST R	ρ = -0.51; p = 0.024	–	–	–
	MD	SLFt L	ρ = 0.57; p = 0.010	–	–	–
	RD	SLFt L	ρ = 0.55; p = 0.014	–	–	–
Expansion	RD	ILF L	ρ = -0.46; p = 0.046	MD	SLFp L	ρ = 0.62; p = 0.005
	–	–	–	RD	SLFp L	ρ = 0.58; p = 0.012
Collier's sign	MD	SLFt L	ρ = 0.46; p = 0.048	–	–	–
Truncal ataxia	AD	FMa	ρ = 0.50; p = 0.029	–	–	–
Limb ataxia	FA	FMI	ρ = -0.54; p = 0.018	MD	ILF L	ρ = -0.69; p = 0.008
Ophthalmoplegia	FA	ILF R	ρ = -0.66; p = 0.002	–	–	–
	RD	ATR R	ρ = 0.56; p = 0.012	–	–	–
Nystagmus	–	–	–	FA	CF R	ρ = -0.50; p = 0.028
Hyperreflexia	FA	SLFt L	ρ = 0.54; p = 0.016	–	–	–
Spasticity	FA	CF R	ρ = -0.50; p = 0.029	–	–	–
		ILF R	ρ = -0.47; p = 0.040	–	–	–
	MD	SLFt L	ρ = 0.47; p = 0.040	–	–	–
	RD	SLFt L	ρ = 0.47; p = 0.040	–	–	–

SOURCE: The authors (2020).

NOTE: * – Spearman's correlation between tracts and clinical data, demographic data and molecular findings (data). Presented as rho (ρ) and p.

LEGEND: FA – Fractional anisotropy; Coef. – Coefficient (FA, AD, MD or RD); R – right; AD – axial diffusivity; MD – mean diffusivity; RD –radial diffusivity; L – left; ILF – inferior longitudinal fasciculus; SLFp – parietal segment of the superior longitudinal fasciculus; SLFt – temporal segment of the superior longitudinal fasciculus; FMa – forceps major; FMi – forceps minor; CF – cingulate fasciculus; ATR – anterior thalamic radiation; SARA – Scale for the Assessment and Rating of Ataxia; CST –corticospinal tract; UNF – uncinate fasciculus.



HIGHLIGHTS

1. SCA3 showed more fiber tracts with changes in diffusivity than SCA10.
2. SARA score was correlated with DTI findings only in SCA3.
3. SCA10 showed myelin-sheath related changes in white matter fiber tracts.
4. SCA3 showed myelin-sheath changes and secondary axonal changes in fiber tracts.